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The Behaviour of the Foetus in Utero with Special Reference to the Incidence of Breech Presentation at Term

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THIS paper is, in some respects, a sequel to one published by the author in 1940[1], in which it was shown that the conditions causing diminution of the pelvic cavity were not the real causes of breech presentation at term. It was, at that time, put forward that the cause should be sought in those conditions which prevented spontaneous version from taking place. In some ways also this paper is an amplification of that theme. In the earlier paper the argument centred around the clinical impression that spontaneous cephalic version tended to take place during pregnancy in breech cases. It was felt necessary to collect more accurate information on this point. While doing this, the contention that breech presentations were not associated with abnormalities in, or of, the pelvis, could be re-tested, as also could the alternative contention that the breech presentation is associated with the extended attitude, with multiple pregnancy, and with prematurity.

The fundamental problem of why the foetus should present by the head rather than by the breech is one which still awaits solution. It has attracted a certain amount of speculation, but the theories advanced to explain it are not convincing. There are the "accommodation" theories, and the theory of gravity.

1. *Accommodation of the foetus to the pelvis.*

Arguing from what is, in fact, a false premise, namely that when the pelvic brim is distorted, or is impinged upon by tumour, the foetus presents as a breech, an explanation is provided in that the circumference of the head is (on average) 13 inches, while that of the breech is only 11 inches. Therefore the latter engages.

Even supposing that the premise were not false, the measurements quoted are of the foetus at term, yet the breech may present at such a stage of prematurity that the head must measure considerably less than the figure given. Furthermore, the ultimate position of the foetus is in most cases decided long before the foetus makes any real attempt to enter the brim.

2. *Accommodation of the foetus to the uterus.*

The uterus is pyriform, wide above and narrow below. Whether the uterine walls can or cannot exert an influence on the position of the foetus will depend on the quantity of liquor in the amniotic sac. Suppose the quantity to be small—then the

narrower end of the foetus accommodates itself in the pelvis, and the wider in the fundus. This might account for the greater incidence of breech in the premature foetus, for the head is relatively larger then than it will be at term. This theory might suffice for the primigravida, though it is difficult to believe that the distended uterus of late pregnancy does control the foetus so accurately, but in the case of the multigravida and in hydramnios it is scarcely tenable.

3. *The gravity theory.*

It is suggested that the head being the heavier end of the foetus, it will naturally tend to turn to a vertex as pregnancy proceeds. Against this, the head is relatively much heavier in the premature foetus than it is at term, yet the breech is much more common before the 30th week than after it. Furthermore the upright position is not constantly maintained by the pregnant woman, yet spontaneous cephalic version will also take place at the appropriate time in a woman confined to her bed for some coincident condition.

None of these theories is good enough, and as stated earlier, the problem still awaits solution.

I have suggested that for some reason, at present unknown, the foetus preferring to be born as a vertex, will undergo a version if it possibly can, and furthermore it will do so at the appropriate time unless it is prevented from doing so. Polak[2] puts the same point thus: "It would have been a head, if it could have been a head." This does not advance our knowledge of why the foetus tends to present by the head, but the corollary suggests why the foetus presents as a breech. The factors which prevent version are the factors which cause the breech presentation (normal earlier), to persist until term.

In the short statistical review published in March 1940,[1] 969 case records of breech deliveries at 5 different maternity hospitals were examined, and it was found that disproportion was present only 13 times (1.3 per cent), and placenta praevia 31 times (3.2 per cent). Anencephaly was present 11 times, and hydrocephalus 9 times. In some of the cases of anencephaly and in many of placenta praevia prematurity was also a factor to be reckoned with, but even disregarding this, a pelvic anomaly could be found only in 6.7 per cent of these 969 breech cases. In the same series it was shown that in 387 cases of placenta praevia the foetus presented as a vertex 356 times, and only 31 times as a breech. In the same series, prematurity was present in 89 cases (9.1 per cent), multiple pregnancy in 229 (23.6 per cent). The extended attitude was recorded 362 times (37.3 per cent). In 222 instances no abnormality was recorded. It was on these figures that I based the hypothesis that the breech presentation should be regarded as a persistence beyond the stage in pregnancy when to present by the breech is normal, and that the persistency is due to those factors which prevent spontaneous cephalic version from taking place.

It has been argued by Gibberd in a personal communication that the foetus extends its legs because it is a breech. This is the "accommodation theory" in another guise, the suggestion being that the foetus, unable to get the breech and feet together into the pelvis, gets the latter out of the way. There is evidence, however, which suggests that the extended attitude of these foetuses is of long standing. He has quoted Trillat's description of two cases of congenital torticollis[3] and attributes this to muscle spasm. In my opinion it is an under-development caused by the head being on one side *in utero* for a long time, and kept in position by the extended limbs. I have seen congenital torticollis in an elderly primigravida delivered by Caesarean section. I have also seen, and a photo-

graph is shown of, a baby in whom the long continued pressure of the extended arm caused a deep indentation of the skull. Chapple and Davidson[4] show that many congenital malformations are associated with the abnormal foetal position *in utero*. They instance congenital dislocation of the hip, hyperextension of the knee ("back-knees"), facial asymmetry, and torticollis. For these gross abnormalities to take place the faulty attitude of the foetus must surely have been of long standing, and have occurred before that stage in gestation when the presence of the feet would make it impossible for the breech also to be accommodated in the pelvis.

To get more light on spontaneous movements of the foetus I set myself the task of documenting my observations on a consecutive series of antenatal patients until such time as the foetus had been observed to present as a breech in 1,000 instances.

Believing that clinical diagnosis could not be made with any certainty in an adequate percentage of cases much earlier than the 30th week, this was about the stage at which I elected to make my first examination. The patients had all been seen earlier than this and any observations then made were used. They were also seen, subsequently, by myself if I wished, and by others if not, and again any relevant data were added. As a check on clinical diagnostic precision, the presentation at birth was also noted. In this way observations covering the whole period when palpation is of value, were gradually accumulated. After 3½ years this part of the task was finished. One thousand breech presentations had been observed after 3,875 patients had passed through our hands, and mainly through my own. Skiagrams were taken if the diagnosis was in doubt, though this was not often. They were also taken in many instances of failed version.

Here then were figures by which certain hypotheses could be checked, upon which observations could be made, and from which certain conclusions could, with justification I hope, be drawn. It may help if at this stage I list these *seriatim*. They will be discussed more fully in the matter which follows.

The Nine Postulates.

(1) The incidence of the breech presentation at the 30th week is high.

(2) In most breech cases, spontaneous version takes place.

(3) Spontaneous cephalic version is a manœuvre which tends to take place once, and once only.

(4) Spontaneous cephalic version is only very rarely followed by a reversion.

(5) Spontaneous cephalic version takes place at a specific time in pregnancy.

(6) Spontaneous podalic version is not common.

(7) External version has a higher reversion rate than has spontaneous version.

(8) Failed version is associated with certain definite clinical findings.

(9) Unheralded breech presentation at term cannot be eliminated, for reasons which will appear later in the text. It too is associated with definite, though different clinical findings.

1. The Incidence of Breech Presentation.

The incidence of breech presentation is high. One thousand breech presentations were observed after 3,875 patients had passed through the clinic.

One woman in 4 therefore is known to have a breech at some time or other. It may well be that an even greater number occur. To prove this would necessitate repeated skiagrams being taken, a formidable task in peacetime, and quite out of the question in time of war. It is hoped that

evidence on this point can be accumulated gradually.

Dearnley[5] with many others agrees "that breech presentation is common till the 34th week."

TABLE I.
Parity and Breech Presentation.

1	2	3	4	5	6	7	8	9	10	11
523	309	85	25	12	4	1	4	1	1	1

Parity does not seem to be an important factor, 523 of the patients were primiparae, 443 were multiparae. (The information as to parity is missing in some of the earlier cases.)

Breech presentation is thus so common that it must be regarded as a normal occurrence at certain stages in pregnancy.

Ryder[6] analysing 1,721 cases finds 272 breeches, an incidence of 1 in 6.

2. SPONTANEOUS CEPHALIC VERSION.

In most breech cases spontaneous cephalic version takes place. This movement was observed on 680 occasions:

TABLE II.

As a single process	599	times
In 5 cases occurring twice	10	,,
Followed by SPV and EV	16	,,
After SPV	11	,,
Followed by SPV and FV	3	,,
After SPV, EV and SPV	1	,,
After SPV and FV	2	,,
After EV and SPV	10	,,
After repeated EV and SPV	2	,,
After FV	26	,,
Total	680	,,

SPV = Spontaneous podalic version
EV = External version
FV = Failed version

Thus in 1,000 cases observed spontaneous version occurs 680 times, and in 599 instances this is the only movement which the foetus is seen to undergo. Of the remaining 81 cases there is clinical interference in 60 instances which makes it impossible to say what would have happened had they been left alone, but as it stands this table shows that spontaneous cephalic version is a movement which only very rarely takes place twice, only 5 times in these 1,000 cases.

The influence of parity seems to be unimportant. In the 599 cases in which the movement of spontaneous cephalic version was the only one known to have taken place, 312 are primiparae, and 287 multiparae.

Polak,[7] criticizing the operation of external version, makes the point that "it would have been a head if it had been left alone."

Taussig[8] states that "with a normal pelvis, normal uterus, and a single foetus,

TABLE III.
Parity and Spontaneous Cephalic Version.

1	2	3	4	5	6	7	8	9	10	11
312	206	55	13	7	1	1	1	1	1	1

gravity and the kicking movements almost always tend to the vertex presentation."

They agree therefore that a vertex usually results spontaneously. Taussig's reasons need further investigation.

Ryder[6] on the other hand found that only 15 out of 258 breeches underwent spontaneous version, but in his series external version was performed 214 times. It seems that Polak was right in suggesting that his figure was lower than it would have been, had the operation been left till later.

Plates 1 to 9 are drawings from skiagrams of foetuses which underwent spontaneous version.

3. THE TIME AT WHICH SPONTANEOUS VERSION TAKES PLACE.

Spontaneous version takes place at a specific time in pregnancy. It is not easy however to elucidate this, for we must face the fact that we do not know exactly how

PLATES 1 TO 9.

Drawings from skiagrams of foetuses which underwent spontaneous cephalic version. All skiagrams taken are shown. It should be noted that the general pattern is one of flexion.

In Plates 1, 3, 5, and 8 ... full flexion.
In Plates 2, 6, and 7 ... semi-flexion.
In Plates 4, and 9 ... extension.

advanced pregnancy is when we examine a patient. We are not dealing with laboratory animals impregnated on a known date. We have to deduce the stage of pregnancy from the date of the last menstrual period. In this series I have deducted 3 months and added 7 days to the 1st day of the last menstrual period irrespective of the particular months involved. When it is noted that a patient is at this or that week it is appreciated that one may be at least 2 weeks out in the calculation. Curiously enough, however, patients do deliver themselves fairly near to the calculated date. I do not believe that the height of the fundus is of any value in this respect. When one pauses to consider that the weight of the foetus at term may vary from 5 to 10 pounds, and that the quantity of liquor may be 2 or 10 pints one realizes the limitations of this observation in assessing the duration of pregnancy in terms of weeks.

The second inescapable fact is that we cannot say when spontaneous version takes place, but only by what date it is known to have taken place.

Subject to these two limitations however it is possible to arrive at an estimated date.

Dearnley[5] states that spontaneous version often occurs up to the 34th week. Ryder notes that it takes place between the 6th and 7th months (presumably between the 27th and 31st weeks). His work was done, however, to eliminate the breech at term, and his external versions were done earlier than in the present series. The bulk of his spontaneous versions were thus anticipated.

In the present series the bulk of the spontaneous versions are known to have taken place by the 34th week. Certainly many have taken place before this, and the figure for those completed by the 32nd week should probably be higher.

Table IV shows that it is most common to find spontaneous version to be completed by the 32nd week, with the 31st and 33rd weeks coming next. These 3 weeks are apparently the critical weeks, and bearing in mind what has been said about the limitations imposed on accuracy, I submit that it will not be easy to fix the date more accurately than this.

TABLE IV.

Showing the Stage of Pregnancy, in Weeks, by which Version is known to have Taken Place.

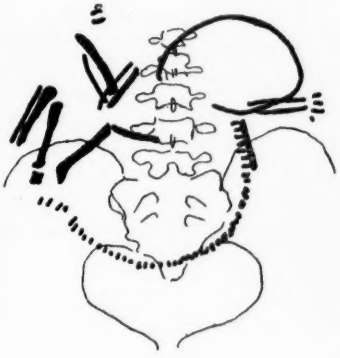
25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
1	1	6	10	19	69	118	133	100	60	18	10	4	1	–	9

4. REVERSION.

Spontaneous cephalic version is only rarely followed by a reversion. This is an important finding, for it is still widely held that the foetus is constantly travelling around in the amniotic sac, and is dependent on "chance," or "gravity" or "frequent kicking movements" for its ultimate position. This is quite certainly not so, for, in this series, while in 599 cases spontaneous version was the only observed movement, in only 25 other cases was this version followed by a reversion to a breech. This suggests to me that the foetus has made a purposive movement, for some definite reason.

The fate of these 25 reversions is as follows: 5 underwent a second spontaneous version; 16 had an external version performed in the interests of the patient; 1 had external version performed twice (we cannot say what would have happened to these 17 had they been left); 3 went to term as breech cases.

The number (25) is too small to study the influence of parity on this tendency to revert. The figures for what they are worth



10

Gravida 3.
EV at 29 weeks.
SPV at 30 weeks.
SV at 33 weeks.
Skiagram at 30 weeks.

11

Gravida 1.
EV at 33 weeks.
SPV at 34 weeks.
SV at 36 weeks.
Skiagram at 34 weeks.

12

Gravida 2.
EV at 32 weeks.
SPV at 32/33 weeks.
EV at 33 weeks.
SPV at 33/36 weeks.
SV at 38 weeks.
Skiagram at 37 weeks.

PLATES 10 TO 12.

From skiagrams of the foetuses which had been subjected to external version, and which had reverted to breech. Plate 11 is from a primigravida. Plates 10 and 12 are from multigravidae. It is seen that the foetuses have more room for movement in these cases. All these subsequently underwent spontaneous cephalic version.

are given in Table V. They seem to show that the manoeuvre is more likely to take place in the multipara.

TABLE V.

	Primiparae	Multiparae	Total
SV. SPV. SV	1	4	5
SV. SPV. EV	6	10	16
SV. SPV. EV repeated	1	–	1
SV. SPV. FV. B ...	2	1	3
Total	10	15	25

SV = Spontaneous cephalic version
EV = External version
FV = Failed version

It is true that the patients were not examined every day, but the impression that these figures reveal the correct state of affairs is strong. Reversions should have been much more commonly observed if they had indeed occurred.

Herbert Spencer observed that after $7\frac{1}{2}$ months the foetus rarely changed its position. We do not know if these were lunar or calendar months; assuming the latter, then one month contains 4 weeks and 3 days approximately, so that $7\frac{1}{2}$ months equals 33 weeks.

Plates 10 to 12 are from skiagrams taken after reversion to breech.

5. SPONTANEOUS PODALIC VERSION.

Spontaneous podalic version was observed to occur 134 times thus:

TABLE VI.

After spontaneous cephalic version ...	25	times
After SCV, SPV, and EV	1	,,
As an initial movement (i.e. reported to be a vertex before the 30th week) ...	45	,,
After one external version	16	,,
In 32 cases of repeated EV	46	,,
After 1 FV, and 1 successful EV ...	1	,,
Total	134	,,

This movement is thus seen to occur 134 times in 3,875 patients or in 3.46 per cent of cases. If then the foetus reaches the 31st to 33rd week as a vertex the chance of this presentation being disturbed is remote.

TABLE VII.

Cases in which Spontaneous Podalic Version was the Initial Movement.

SPV. SV	11
SPV. EV	20
SPV. EV. SPV. SV	1
SPV. FV. SV	2
SPV. FV. B	4
SPV. B	7
Total	45

It was noted to occur as an initial movement on 45 occasions; one quarter of these readjusted themselves. Half were corrected and again we cannot say what would have been their fate. The remaining quarter went to term as a breech (Table VII).

The details are here given of the 11 cases in which spontaneous podalic version occurred, and when the patient went to term as a breech (Table VIII).

The details of those starting with an SPV and of those cases in which an SPV was noted, but which were subsequently delivered as a vertex, have not been extracted from the records.

Randall[9] suggests that an X-ray photograph should be taken after a spontaneous podalic version "as an anomaly of the foetus may be detected."

In this series, with the exception of the first, there is no suggestion of any factor influencing the foetus.

6. External Version and Reversion.

External version has a higher reversion-rate than has spontaneous version; a fact which suggests that the obstetrician is not so clever as the foetus in deciding when the operation should be done. The inability to date the stage of pregnancy accurately is one factor in this.

In this series the operation was performed 330 times (Table IX).

In the categories marked with an asterisk, this interference was successful, and no reversion occured (223). In the categories marked † the final EV was successful (35). The total number of ultimately successful external versions is thus 258. In the remaining cases something else happens afterwards. The reversion-rate is thus 22 per cent approx.

Ryder[6] finds also that one third of the

TABLE VIII.

Number	Age (years)	Gravida	Vertex noted	Breech first noted
1090	23	1	34	42 (anencephaly and spinabifida)
477	33	1	30	39
332	19	1	40	40
994	29	1	33	38
1155	30	1	36	37
368	37	2	29	33
667	25	1	36	37
1122	23	1	31	35
828	21	1	33	38
671	44	3	36	38
1404	23	1	34	40

Photograph of a baby born as a breech with extended limbs. There is marked compression of the skull, and facial asymmetry.

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external versions performed will revert (33·3 per cent).

McGuiness[10] in a short series shows 12 reversions in 57 external versions (21 per cent).

The weeks at which a successful and final version was performed in the above mentioned 258 cases as shown in Table X. The weeks at which external versions are done in those cases where the cephalic position is not maintained is also shown. Table XI.

TABLE IX.

*SV. SPV. EV		15
†SV. SPV. EV. repeated once ...	1	2
† do. do. repeated thrice ...	1	4
*SPV. EV		20
SPV. EV. SPV. SV		1
*EV		176
EV. SPV. SV		10
†EV. repeated once	23	46
†EV. repeated twice	6	18
†EV. repeated thrice...	3	12
EV. repeated once, SPV. SV ...	2	4
EV. SPV. B		6
*FV. EV		12
†FV. EV. repeated thrice	1	4
Total		330

SV = Spontaneous cephalic version

Examining Table XI it is seen that the incidence of reversion begins to fall off after the 33rd week.

This can also be expressed in percentage by combining Tables X and XI.

The tendency is for a high percentage of versions performed early to revert, while after the 31st week this tendency falls off.

7. FAILED VERSION.

Failure to turn the breech to a vertex occurred on 77 occasions, thus:

TABLE XIII.

SV. SPV. FV. B	1
SPV. FV. SV	2
SPV. FV. B	6
EV. SPV. FV. B	3
FV. SV	26
FV. EV	12
F.V. repeated	1
FV. B	26
Total	77

The failure was subsequently overcome, spontaneously 28 times, and by the obstetrician 13 times. In the remaining 36 instances the patient was delivered as a breech.

Plates 13 to 16 are of drawings from skiagrams of foetuses in which version failed,

TABLE X.

22	23	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
1	1	4	2	9	7	11	14	49	47	36	29	28	10	5	2	3

TABLE XI.

Week	27	28	29	30	31	32	33	34	35	36	37	38	39
Number	1	1	4	5	10	11	16	10	5	4	2	2	1

TABLE XII.

Week	22	23	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Finally successful version	1	1	4	2	9	7	11	14	49	47	36	29	28	10	5	2	3
Version not final				1	1	4	5	10	11	16	10	5	4	2	2	2	1
Approximate percentage of versions which are not final				33	10	36	31	41	18	25	21	15	13	16	28	50	25

13

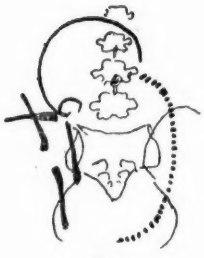
Gravida 1.
FV at 33 weeks.
SV 33/34 weeks.
Skiagram at 33 weeks.

14

Gravida 1.
FV at 34 and 36 weeks.
SV 36/40 weeks.

15

Gravida 1.
FV at 31 weeks.
Skiagram at 33 weeks.
SV at 33/34 weeks.



16

Gravida 1.
FV at 34 weeks.
Skiagram at 35 weeks.
SV 35/40 weeks.

PLATES 13 TO 16.

From skiagrams taken after failed version. In all these cases spontaneous version followed.

The attitude is extension in 13, 14, and 16.
The attitude is flexion in 15.

and in which spontaneous version subsequently occurred (FV. SV.).

There were 2 stillbirths. In No. 4 Spalding's sign was noted when she was X-rayed and she delivered herself of a macerated hydrocephalic. In No. 22 the mother had albumen "++" in the urine, and BP 165/120 (see Table XIV).

Vaginal bleeding occurred after attempted version in Cases 18 and 35.

Very little liquor was noted in Cases 3, 9, 27.

Case 29 was a multiple pregnancy.

Case 23 was the patient's 2nd breech delivery.

The table of cases of failed version result-

TABLE XIV.

Details of Breech Deliveries after Failed Version (36 *cases*).

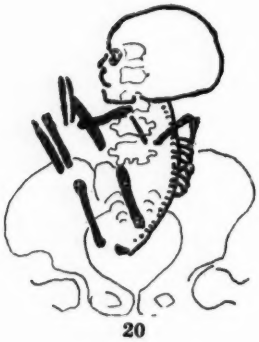
No.	Case number	Age (years)	Gravida	Maturity (weeks)	Weight of baby lb.	oz.	Attitude	X-ray	Anaesthetic	Treatment	Fate of baby
1.	998	22	1	38	5	12½	Extd. legs	o	+	ARM	A
2.	69	28	1	40	6	7½	do.	+	o	ARM	A
3.	1137	35	1	38	3	10	do.	+			A
4.	498	19	1	35	7	o	do.	+			SB
5.	856	23	1	40	6	15	do.	+	+		A
6.	1389	24	1	38	6	1¾	do.	+			A
7.	16	22	1	39	6	o¾	do.	+	+		A
8.	85	26	1	39	7	1½	do.	+		ARM	A
9.	214	26	1	38	6	2	do.	+			A
10.	470	30	1	39	7	1½	do.	+			A
11.	1105	29	1	39	7	o¾	do.	+		ARM	A
12.	105	27	1	40	6	4½	do.	+		ARM	A
13.	202	20	1	38	5	7	Well flexed	+	+	ARM	A
14.	994	29	1	39	6	3				M.Ind.	A
15.	368	37	2	40	7	o¾			+	M.Ind.	A
16.	1022	23	1	37	6	3					A
17.	636	20	1	37	6	o¼					A
18.	160	29	1	36	5	5¾			+	ARM	A
19.	740	32	1	38	6	2			+	ARM	A
20.	325	26	1	40	7	13¾					A
21.	576	28	2	38	6	10½	Ext. limbs	+		ARM	A
22.	735	27	1	39	6	6½	1 arm and 1 leg extd.	+			SB
23.	896	25	2	35							A
24.	706	34	1	37	6	8½	Extd. legs			ARM	A
25.	862	25	1	36	6	1	do.				A
26.	1123	20	1	37	7	o¼	do.	+		M.Ind.	A
27.	1052	29	2	40	7	1¼	do.				A
28.	157	28	1	40					+		A
29.	1011	29	1	40	5	3¼					A
30.	825	21	1	—							
31.	671	44	3	40	6	3½				M.Ind.	A
32.	1404	23	1	40	7	11	Extended				A
33.	1110	16	1	38	6	8½	Semi-extd.	+			A
34.	358	30	2	37	6	8½	Extd. legs	+		ARM	A
35.	1018	30	5	38	7	13½					A
36.	611	29	1	38	6	9					A

\+ = Skiagram taken, or anaesthetic administered for version.
A = Born alive.
ARM = Artificial rupture of the membranes.
M.Ind. = Medical induction.

17

18

19



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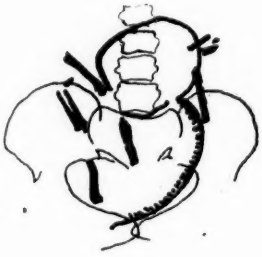

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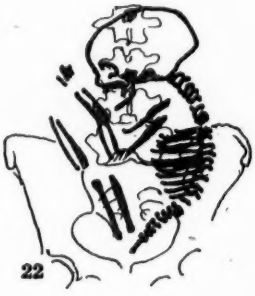

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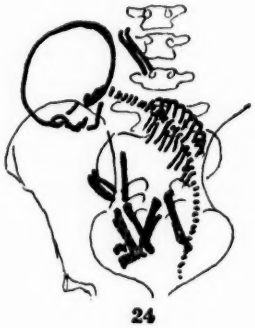

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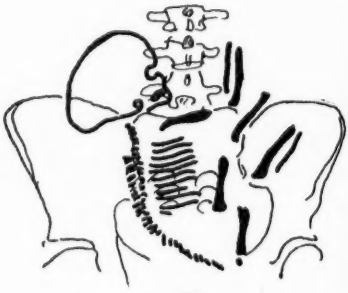

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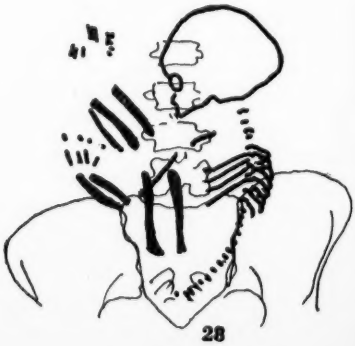

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PLATES 17 TO 33.

From skiagrams taken after failed version. Breech persists till delivery.

The attitude is extension in:

17, 18, 20, 21, 22, 26, 28, 29, 30, 31, 32, 33.

The attitude is semi-extension in:

19, 23, 25, 27.

The attitude is flexion in 24.

The particularly upright stance in numbers 19, 20, 26, 27, 28, 29, 30 and 31 should be noted. It indicates a tight application of the uterus to the foetus and means that the quantity of liquor is small.

ing in breech delivery at term shows that in 20 of the 36 cases the attitude was extension, and in 1 other, semi-extension. Confirmation was made by skiagram in 16 instances, in 4 others the observation was made at delivery. In 15 cases there is no note of the attitude of the foetus.

Very little liquor was estimated to be present in 3 of the cases.

There was 1 instance of multiple pregnancy.

Five were multiparae and the remainder primiparae. (In 2 instances the information is lacking.)

An anaesthetic was administered for attempted version in 9 cases.

Reproductions of the skiagrams are shown (Plates 17 to 33).

Breech Deliveries.

The number of women who were known to have a breech presentation at some time or other in their pregnancy and who were subsequently delivered as a breech was 85, or 8.5 per cent. The other 91.5 per cent are eliminated. This figure of 85 is made up as shown in Table XV.

Table XV.

SV. SPV. FV. B	1
SP. FV. B	6
SPV. B	5
EPV. B	2
EV. SPV. B	3
EV. SPV. FV B	3
F.V. B	26
B	39
Total	85

EPV = External podalic version.

Table XVI.

Unheralded Breech Deliveries (32).

Number	Age (years)	Parity	Maturity (weeks)	Baby's weight lb.	oz.	Attitude	Notes	Result to baby
723	23	1	39				1st of twins	A
843	23	1	35	1	14		1st of twins; macerated	SB
				2	7		2nd of twins; macerated	SB
63	31	1	38	5	0¾		2nd of twins	A
114	25	1	40	v.small			Macerated	SB
162	37	4	36	4	6		Maternal BP 180/120 ARM	A
974	24	1	38	7	2	Extended	Very little liquor	A
825	23	1					Transferred	
1238	22	2	36	4	1		1st of twins	A
1271	28	2	37				Macerated, small placenta	SB
1223	37	3	29	2	4		Premature	D
1274	26	3	40	6	13		1st of twins	A
870			34				Transferred	
7	21	2	31				Premature	SB
203	25	1	41	7	2½		Hydrocephalus; spinabifida	A
872	21	1	40	5	3	Extended	Spinabifida; talipes	SB
1229	32	1	40	6	1½	Extended	Undiagnosed	A
415	27	1	32	5	7		Macerated; anencephalic	SB
541	34	2	36	4	12½		2nd of twins	A
578	27	2	38	5	6		2nd of twins	A
684	26	2	38	6	2		1st of twins	A
960	30	2	38				One of twins	A
411	42	1	36	4	4		2nd of twins	A
283	27	1	26	not weighed			1st of twins	SB
							2nd of twins	SB
1199	37	2	38	7	11		2nd of twins	A
939	26	2	40	6	2½		Hypospadias	A
365	32	1	40	5	0		2nd of twins	A
1042	35	5	26				Macerated; premature	A
178	37	3	30	2	7		Placenta praevia	SB
73	35	5	36	8	1¼			A
1044	24	2	42	7	1¾		Little liquor	A

With the exception of the external podalic versions followed by breech delivery, and of the cases of breech delivery without any recorded movements, either spontaneous or induced, these breech deliveries have been described earlier in the text. It remains only to enlarge upon these two exceptions.

External Podalic Version (2).

There were two cases in which this operation was performed. One was previously a brow presentation in a primigravida, the other was a sextipara with an oblique lie (Table XVI).

In addition to these 32 cases, there were 7 others the notes of which could not be traced. One was known to be a case of twins, and 1 a premature.

Rearranging Table XVI we see that the 32 breeches are made up as follows:

One of twins	15
Premature or macerated	6
Spinabifida (1 with hydrocephalus)	2
(Anencephaly also macerated 1)	
Nothing unusual	4
Information lacking	2
Little liquor	2
Placenta praevia	1

There was 1 placenta praevia. The foetus was also premature.

Stillbirths.

In Table XVI, where the information of 32 breech deliveries is complete, there are 11 stillbirths.

They are made up as follows:

Macerated foetus	5
Premature	5
Abnormal foetus	1

One premature baby died subsequently.

In Table XVI, where the information of failed version there were 2 stillbirths, 1 was macerated, and in the other case the mother was severely toxic.

In the whole series therefore 13 stillbirths and 1 neonatal death occur. In 13 of these the chance of survival was hopelessly prejudiced. In the remaining 1 the maternal toxaemia must have prejudiced the chance of survival. There was no other foetal death. Fourteen foetal deaths thus occur in 87 cases (16 per cent).

As only 1 of these could have survived, the "delivery mortality" is 1.14 per cent or nil, according to how the influence of the maternal toxaemia in Table XIV, No. 22, is assessed.

Discussion.

It is probably agreed that the incidence of breech at some time or other in pregnancy is high. It was surprising to find it so high, but as the notes of all patients passing through the clinic during the period of the investigation were perused, and the information used whether or not the patients had been seen personally, the question of selection is eliminated.

Breech presentation is regarded with too much apprehension by the patients. It should be possible, however, if medical students and midwives are correctly taught, to build up the concept that this presentation is normal at a certain stage in pregnancy. Such phrases as "the baby is upside down" (when incidentally it is in the position we all prefer), and that "the baby is the wrong way round," should disappear. No good can be done by causing an antenatal patient to think that there is something wrong, or that she is abnormal.

From the figure given earlier it can be anticipated that spontaneous version will take place in 3 out of 5 patients. The patients can be told this and they will look forward to having this confirmed at their next visit.

Why spontaneous version takes place requires further investigation. The fact that

it is usually a solitary movement, and that it takes place at a specific time in pregnancy, is against its being a purely chance phenomenon. If it is due to gravity then it would have to be shown that the specific gravity of the foetal head becomes progressively greater than that of the caudal end. This still would not explain why version takes place in the recumbent patient, or why the new position is sometimes reversed again.

Why spontaneous podalic version takes place is also an interesting speculation. It does not occur often enough to lend support to the theory that the foetus is constantly changing its position, and that therefore the choice of heads or tails at term is decided by chance. It is worthy of note that it happened in only 25 instances after spontaneous version, whereas it occurred 64 times after external version. It could be inferred that if the conditions necessary for cephalic version are not present then reversion may take place after an external version prematurely performed.

Why spontaneous cephalic version does not take place is more easily elucidated. Examination of Tables XIV and XVI, where the details of 68 cases are set out, shows the following facts:

Extended attitude of the foetus (5 times associated with little liquor)	23
Twin pregnancy	17
Premature and/or macerated	7
Abnormal foetus	3

In 50 out of the 68, therefore, there is something to consider, and it seems justifiable to postulate that, in the premature and the abnormal foetus, the conditions necessary for spontaneous version have not yet occurred, and that, in the cases in which the limbs are extended and when there is little liquor, the foetus can no more get round than can the obstetrician force it round. When twins are present the foetuses may mutually prevent each other from turning.

In this series these are the causes of the breech presentation. Contracted pelvis, fibroid or ovarian cyst were not found. Only 1 placenta praevia was noted and prematurity was a coincident factor.

Stein[11] of Chicago notes the frequency of the extended attitude in breech cases, and its relative infrequency in vertex cases and has speculated that this may be one of the causes of breech presentation. He points out that in an analysis of skiagrams taken in late pregnancy, and in labour, the attitude of deflexion is the rule.

Henderson[12] of Detroit found "the extended attitude" (meaning extended legs) in approximately 75 per cent of cases.

When spontaneous cephalic version does not take place it can be assumed that either there is very little liquor, or that the limbs are extended. If facilities are available this last point is easily checked.

When performing external version, the conditions *in utero* must be kept in mind. The emphasis should be laid on inducing the foetus to undo its extension, and to turn rather than on the attempt to force around an inanimate object of the wrong shape. The foetus will respond to stimuli as Barcroft[13] and others have shown. Gentle pressure on the cephalic end will nearly always induce vigorous movements. This may well undo the extended attitude, and the foetus, "taken unawares," may be moved around partly or wholly. The foetus should be taken around the way of least resistance. There is no need to fear causing the extended attitude; that is there already. As the foetus is most responsive to pressure on its facial aspect, turning it backwards is often successful when forward or orthodox version fails and was advocated by Spencer[14] in 1901 though based on an experience of only 6 cases. Only one pole should be pressed upon at a

time to allow the foetus to bulge out the uterus at the other. The operation must never be so violent as to distress either mother or foetus, and it can be repeated every week or oftener if it is thought necessary, until the final decision is reached.

Anaesthesia is unlikely to help in most cases. Patients are taught the virtues of relaxation antenatally as a preparation for their labour, and much better relaxation can be achieved with a patient's intelligent co-operation than will be obtained with anything short of deep anaesthesia. When this deep anaesthesia has been obtained, the temptation to overcome the obstinacy of the foetus is too great for many to resist; and that way lies disaster. Wrigley[15] gives the appalling infant mortality figure of 13 per cent after external version under anaesthesia. In this series it was only employed when the patient was intolerant of any attempt being made without. It was used 9 times in 392 attempted versions. No foetal death occurred.

Antepartum haemorrhage (accidental) occurred twice. Once very slightly at the time of a version under anaesthetic; once a fairly considerable loss occurred in a patient who had had an external version 10 days previously without an anaesthetic.

If the breech delivery is conducted by an experienced obstetrician or midwife, then the mortality does not seem to be any higher than in the case of the vertex. The breeches which are lost by the experienced are often cases of dystocia. Breech foetal survival should be compared with the survival rates of the vertex in dystocia if a correct sense of proportion is to be maintained.

It is when difficult delivery is added to the unusual presentation, that the mortality begins to go up. It is incumbent therefore on the obstetric team to see that no woman who has a persistent breech shall also be asked to deliver herself of a large baby which we also know from experience will in the great majority of cases be in the extended attitude.

If the baby seems large or the pelvis small, then failure to eliminate the breech by the 38th week, is strong indication for the induction of premature labour, or, if it is held that even then the foetus is too large for comfort, the indication is for planned Caesarean section at term.

This plan has been followed in this series. Of the 38 persistent failed versions, 4 were medically induced, and 11 surgically by the rupture of the membranes. One Caesarean section was performed. In the remaining 22 the size of the foetus, and the capacity of the pelvis were correctly judged to allow of a good prognosis being given and no interference was necessary. Seven pounds 13 ounces in a primigravida, and 8 pounds $1\frac{1}{4}$ ounces in a multigravida, were the heaviest babies born as a breech.

The weight groups were as follows:

Pounds	Pounds	Pounds	Pounds	Pounds
3 to 4	4 to 5	5 to 6	6 to 7	7 to 8
1	0	4	18	10

The deliveries were conducted by the rotation method described by Løvset[16] of Bergen, and in most cases the forceps was applied to the after-coming head.

The Skiagrams.

Examination of the drawing of the skiagrams shows that when the foetus eventually turns the attitude is for the most part flexion or semi-flexion, whereas when the foetus resists version the attitude is most often extension. The quantity of liquor in the uterus can also be gauged by the stance of the foetus.

It is also seen, however, that it is not possible to say from the examination of a

photograph, what will happen, but only what is most likely to occur.

Summary.

By way of summarizing, I return to my nine postulates.

Breech presentation in pregnancy is so common that at the appropriate stage it is normal. It is the persistence beyond this stage that constitutes the abnormality.

In 60 per cent of cases spontaneous version will take place.

Once it has taken place reversion only very seldom takes place.

Version is shown to be most often completed by the 32nd week.

External version as a therapeutic measure is therefore indicated for the breech persisting after the 32nd week.

Failed version usually means little liquor and an extended attitude.

These two factors therefore stand out as the real aetiological factors of breech presentation at term.

Multiparity and prematurity are also factors.

The clinical work upon which this paper is based was done at The British Hospital for Mothers and Babies at Woolwich.

In January 1941, when the maternity department at the Memorial Hospital, Woolwich, was shut down, I asked permission to see antenatal cases at this hospital. Not only was permission graciously given by Miss Gregory and Miss Cashmore, but the utmost assistance was afforded to me by the staff there, all very experienced midwives, among whom I would particularly thank Sister Nield, and Sister Grose for the help they have given me. I have been able to use the observations made by the other physicians; their notes were an indispensable supplement to my own, and I am very grateful to them for their assistance.

Dr. Eileen Wise was in charge of most of the deliveries. The fact that the only babies which were lost in this series were 5 macerated, 6 premature, and 1 abnormal foetus, is a tribute to her obstetric skill, and I record my profound admiration for it.

I am also grateful to Professor Browne for reading through this paper prior to its publication and for his helpful criticism.

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Body Temperature—A Diagnostic Aid in Menstrual Disorders and Sterility

BY

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As early as 1904 Van der Velde[1] discussed the variations in body temperature which occur during the menstrual cycle. In the last few years additional evidence of the diagnostic value of body temperature graphs has accumulated.

Palmer[2] made observations on 35 normally menstruating women during 130 complete cycles. The temperature graphs showed usually a constant biphasic curve with a relatively constant luteal phase, independent of the length of the cycle. The patients took the rectal temperature every morning on awakening. In no case observed was there any discrepancy between the phase of the cycle as indicated by the basal body temperature curve and the endometrial specimens. The following observations were made:

Secondary amenorrhoea due to persistent follicular activity (as confirmed by endometrial biopsy). Basal body temperature persistently low.

Secondary amenorrhoea due to primary pituitary dysfunction. Basal body temperature higher without fluctuations (similar to the type seen in menopausal women).

Oligomenorrhoea (1½ to 6 months cycles): Basal body temperature showed a constant rise 14 days before menstruation.

Onset of pregnancy: Basal body temperature showed sustained temperature elevation.

Martin[3] had 99 patients taking the vaginal or rectal temperature during 181 cycles. The temperature graphs of normal menstruating women showed a constant biphasic curve with a constant luteal phase. Fluctuations of temperature occurred between 0.3°F. and 1°F. with the following changes during the menstrual cycle:

Premenstrual phase. Fall of temperature.

Menstrual phase. Low temperature.

Oestrogenic phase. Low temperature.

Ovulatory phase. Sudden rise of temperature.

Luteal phase. Sustained elevation of temperature.

He observed that injections of oestrogen lowered the basal body temperature, whereas injections of progesterone raised the basal body temperature.

Williams[4] investigated the basal body temperature of 35 women during 2 months, in correlation with their basal metabolic-rate and found temperature variations during the cycle to be between 0.9°F. and 1.6°F. with a low point of temperature on the day of ovulation. He could not detect any correlation between basal body temperature and basal metabolic rate.

Lyon[5] investigated the basal body temperature in cases of functional dysmenorrhoea during 127 cycles in 30 females aged 16 to 34 years, and noted the characteristic rise in the temperature curve preceding each flow when pain occurred. When occasionally the temperature curve lacked the premenstrual rise, and thus labelled a cycle as non-ovulatory, dysmenorrhoea did not occur in that cycle. Lyon con-

cludes that a progestational endometrium is necessary for the typical cramps of functional dysmenorrhoea, and that the basal temperature curve can be of help in differentiating functional dysmenorrhoea from other kinds of menstrual pain.

Tompkins[6] corroborates the findings of others and reports coitus or artificial insemination leading to successful pregnancies when practised on the sudden rise of temperature after its previous low drop during the midcycle.

Investigation of Vaginal and Oral Temperature Curves in 41 Women During 150 Cycles.

Experimental Procedure.

The 41 women comprised subjects with normal cycles, menopausal patients, and patients suffering from various forms of primary and secondary amenorrhoea, menorrhagia, intermenstrual bleeding and dysmenorrhoea. The effects of oestrogen, progestogen, androgen and vitamin B administration on the temperature curve were investigated. All women took vaginal, oral or both temperatures simultaneously every day at the same time, usually in the evening.

Results.

Women with normal cycle (Fig. 1). Twenty-three cycles were investigated.

Premenstrual phase. Fall of temperature about 1 or 2 days before menses.

Menstrual phase. Further decrease of temperature which may reach a level as low as 97°F. followed by a rise to about 98°F. or 99°F.

Fig.1

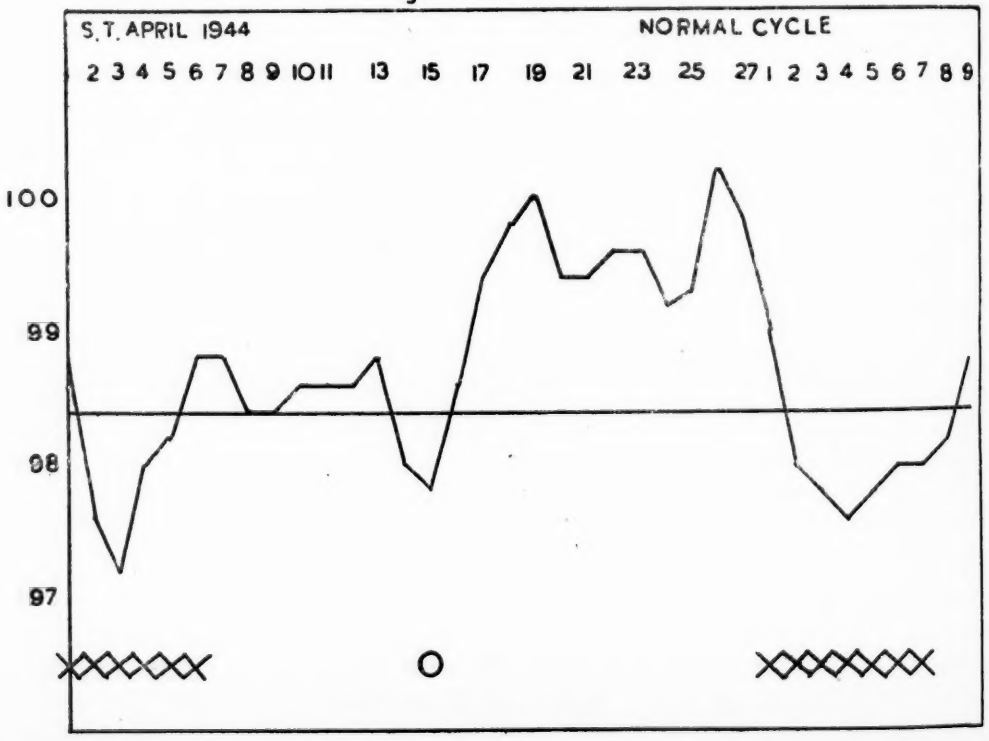
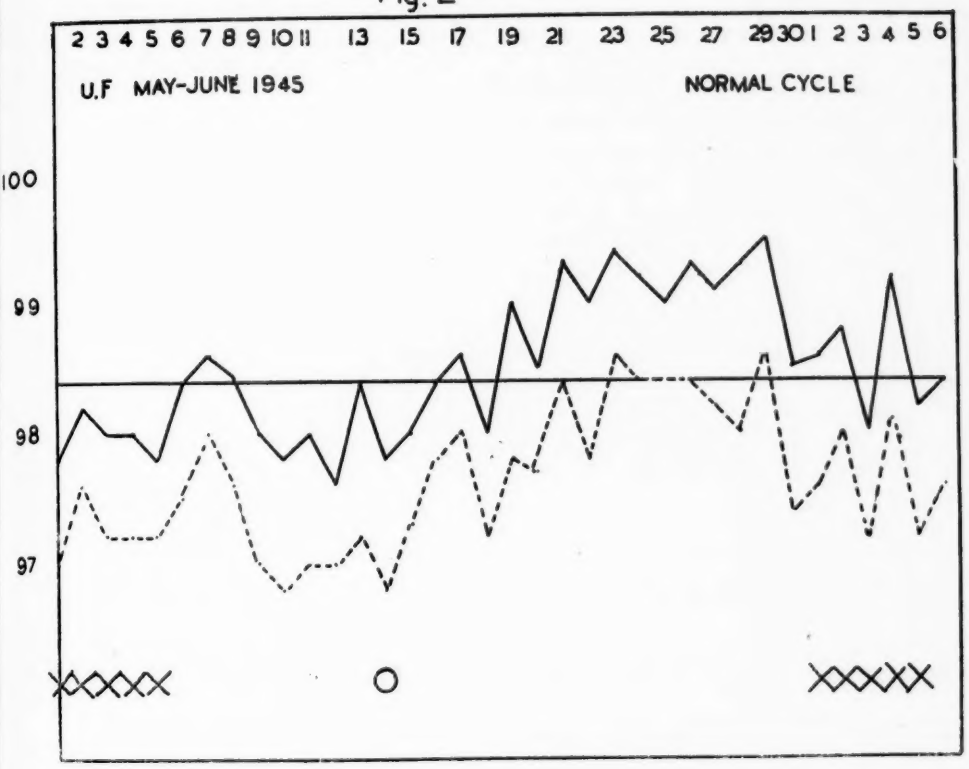


Fig. 2



Follicular phase. This phase is characterized by a low fluctuating temperature of approximately 98.4°F. to 99°F.

Ovulatory phase. In normal women a sudden fall of temperature usually occurs on the 14th day before the onset of menses. It sometimes reaches a point as low as 97°F. followed by a sudden rise.

Luteal phase. A sustained elevation of temperature reaching 100°F. or higher, continuing until about 1 or 2 days before the menses.

Mid-luteal phase. A slight decrease of temperature takes place at this phase, corresponding with the oestrogenic peak.

Oral and Vaginal Temperature.

Thirty-four cycles have been observed of patients taking oral and vaginal temperatures simultaneously, and these temperature curves in all cases show an almost identical pattern. Rise and fall of vaginal temperature is almost always accompanied by a rise and fall in oral temperature. The follicular, ovulatory and luteal phases are well expressed by the oral temperature (Fig. 2). In the normal woman the difference between oral and vaginal temperature taken in the evening is about 0.6°F. to 0.12°F. (Fig. 2). This difference may decrease or increase, or disappear completely in various forms of genital hypoplasia (Fig. 3). The curves of morning

temperature differ from those taken in the evening, particularly when the patient is given treatment which elicits temperature changes (Fig. 4).

Although the temperature curves are of the same pattern, the oral and vaginal temperatures react differently to oestrogen and progestin. Each of the hormones acts individually, producing curves of different height, a fact which greatly facilitates the diagnosis of functional disorders.

Progestin in Presence of Oestrogen.

Observation of vaginal and oral temperature curves (both temperatures taken simultaneously) throughout many cycles has revealed that progestin administration in the presence of oestrogen produces a greater increase of vaginal than of oral temperature. Although both oral and vaginal temperature curves rise, the distance between the curves increases (Fig. 5.)

Oestrogen.

The administration of oestrogen, on the other hand, produces a greater decrease in oral than in vaginal temperature (Figs. 6 and 7). Thus, both progestin in presence of oestrogen, and oestrogen increase the distance between the oral and vaginal curves.

Progestogen in Oestrogen Deficiency.

Administration of progestogen in the absence or relative deficiency of oestrogen,

Fig. 3

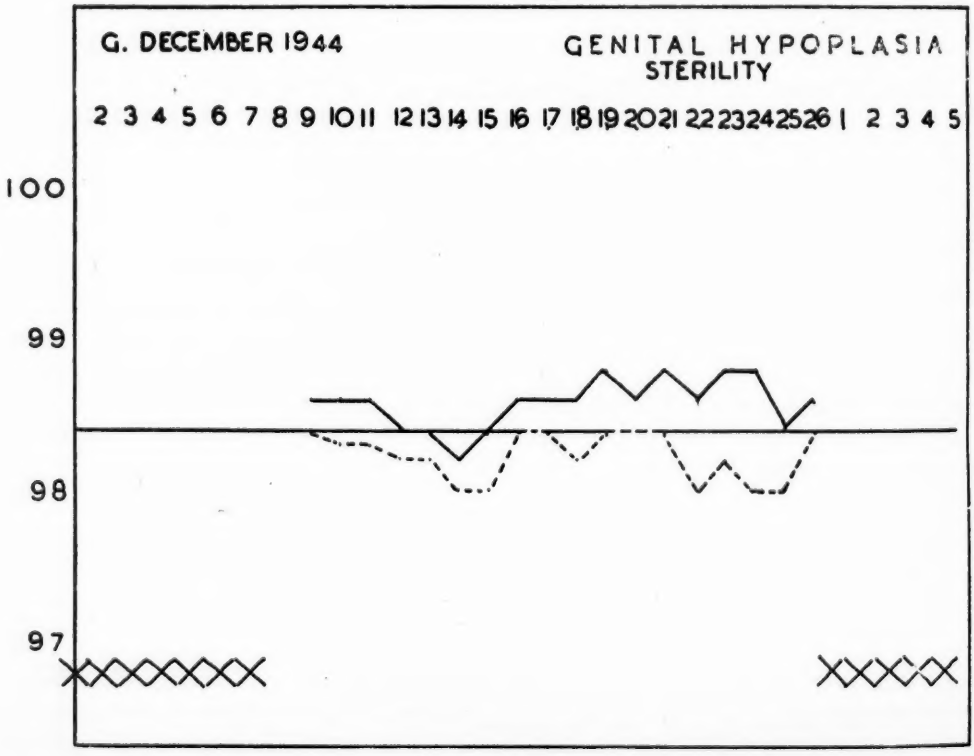
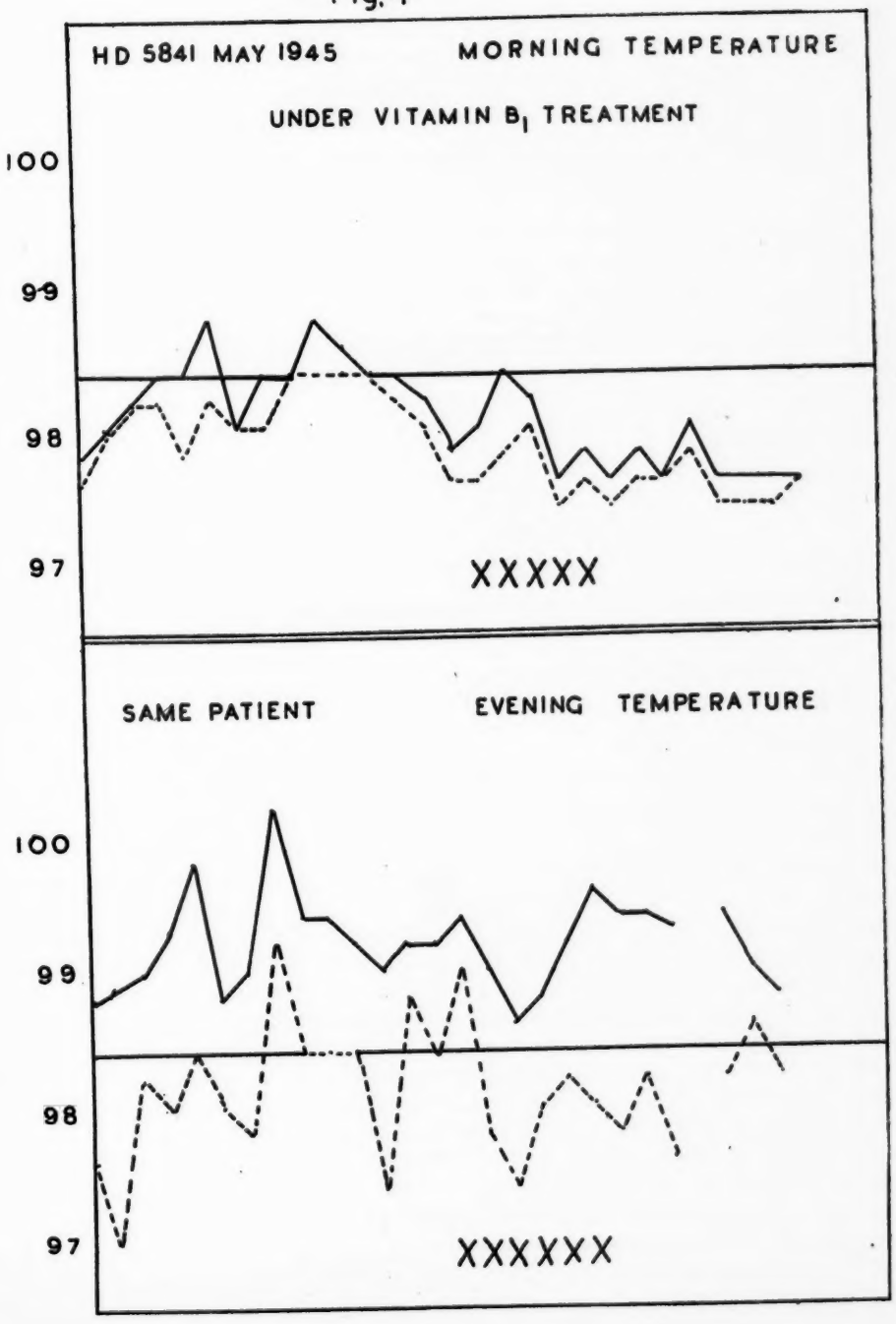


Fig. 4


HD 5841 MAY 1945
MORNING TEMPERATURE
UNDER VITAMIN B1 TREATMENT
100
99
98
97
XXXXX
SAME PATIENT
EVENING TEMPERATURE
100
99
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97
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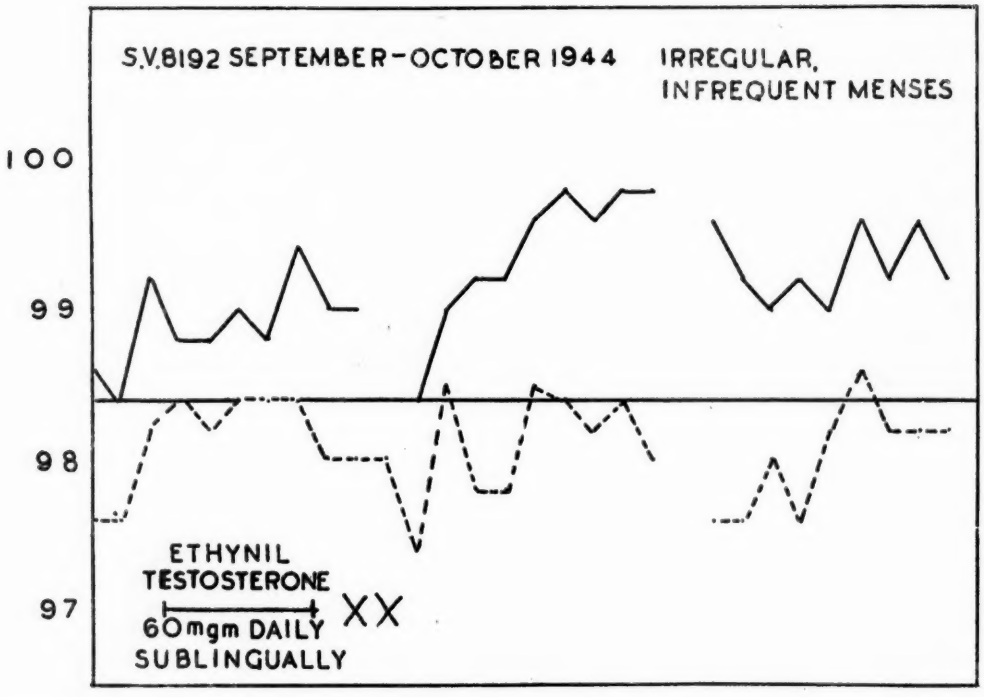
Fig. 5



has a greater effect on the oral than on the vaginal increase of temperature, causing an approximation of the curves (Fig. 7). The oral curve, free from the temperature lowering action of oestrogen, rises at a relatively greater rate towards the level of the vaginal curve. The oral curve rises proportionately to the relative or absolute state of oestrogen-deficiency, and may reach the level of the vaginal curve and be separated only after renewed oestrogenic activity occurs, or progestin withdrawal takes place (Figs. 6 and 8).

Both progestogen and oestrogen increase the distance of the temperature curves, progestogen with predominant action on the vaginal temperature, and oestrogen dominating the oral temperature.

Secondary Amenorrhoea.

The temperature in cases of secondary amenorrhoea due to protracted follicular activity, either of polyfollicular or hyperfollicular nature, shows a persistently low curve, either fluctuating or constant (Figs. 11 and 12). It is tempting to associate the constant low temperature with hyperfollicular amenorrhoea and the fluctuating low temperature with polyfollicular amenorrhoea. A higher temperature curve frequently observed in secondary amenorrhoea, is presumably due to pituitary failure or persistent luteal activity, or both (Fig. 10).

Oligomenorrhoea.

The follicular phase is prolonged and

menses occurs 14 or more days after ovulation (Fig. 8).

Menorrhagia.

There is constantly a prolonged follicular phase with delayed ovulation and short luteal phase (Figs. 11 and 15).

The temperature, however, does not fall as normally in the premenstrual phase, but remains on a high level until the end of the menstrual phase.

Dysmenorrhoea.

Thirty-eight cycles were examined and all showed a lack of the normal oestrogenic fall of temperature one or two days before onset of menses. On the contrary, a rise of temperature occurs which decreases only at the end of menstruation or after menstruation has ceased (Figs. 6, 8, 14, 15 and 16).

Patients taking both oral and vaginal temperatures show a rise of both curves prior to menstruation.

The oral temperature, however, increases at a greater rate than the vaginal, approaching and finally reaching the level of the vaginal curve before or during menses. Renewed oestrogenic activity lowers both curves with predominant action on the oral temperature so that the distance between the curves again increases (Figs. 6 and 8).

Fig. 6

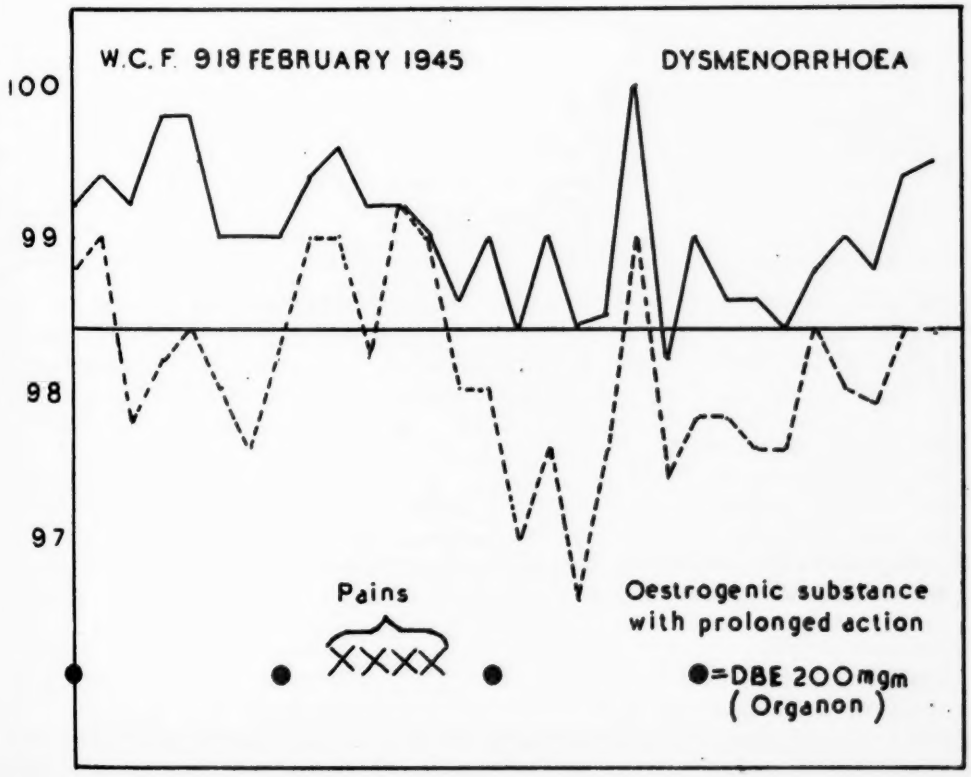
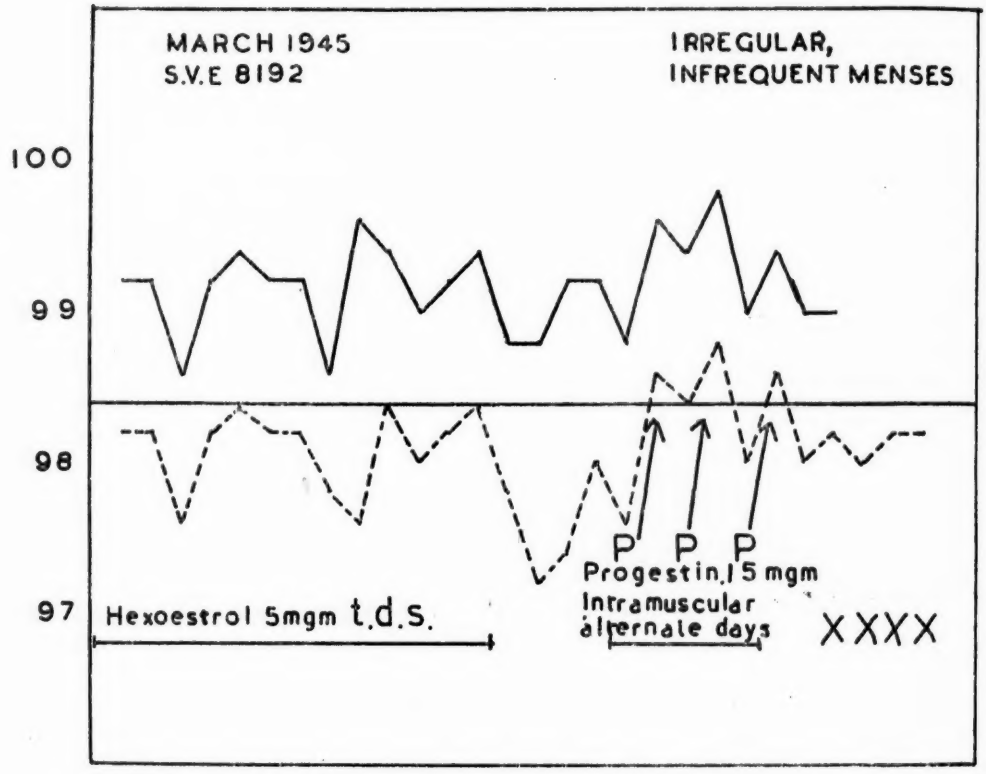


Fig. 7



An exacerbation of pain was noted in those cycles in which such approximation or union of the curves occurred (Figs. 6 and 8).

Intermenstrual Bleeding.

Patients suffering from intermenstrual bleeding show a relatively high temperature curve with only minor fluctuations. Bleeding each time is associated with only slight increase in temperature (Fig. 17).

Menopause.

The temperature during the menopause may be either high or low, and always shows a constant pattern or with very slight fluctuations (Fig. 18).

Oestrogen Administration.

Administration of oestrogen always produces a lowering of temperature, frequently producing a characteristic curve of marked up-an-down fluctuations of 1°F. and more (Figs. 19 and 20).

It is interesting to note that this characteristic curve of marked up-and-down fluctuation in some cycles occurs about 12 days after the beginning of oestrogen administration, lasting about 12 to 14 days. In other cycles it may start 12 to 14 days followed bya sustained rise of temperature.

Oestradiol benzoate 60,000 units intramuscularly injected in 3 doses of 20,000 I.B.U. over 2½ hours into a menopausal woman produced a decrease of temperature

Fig.8

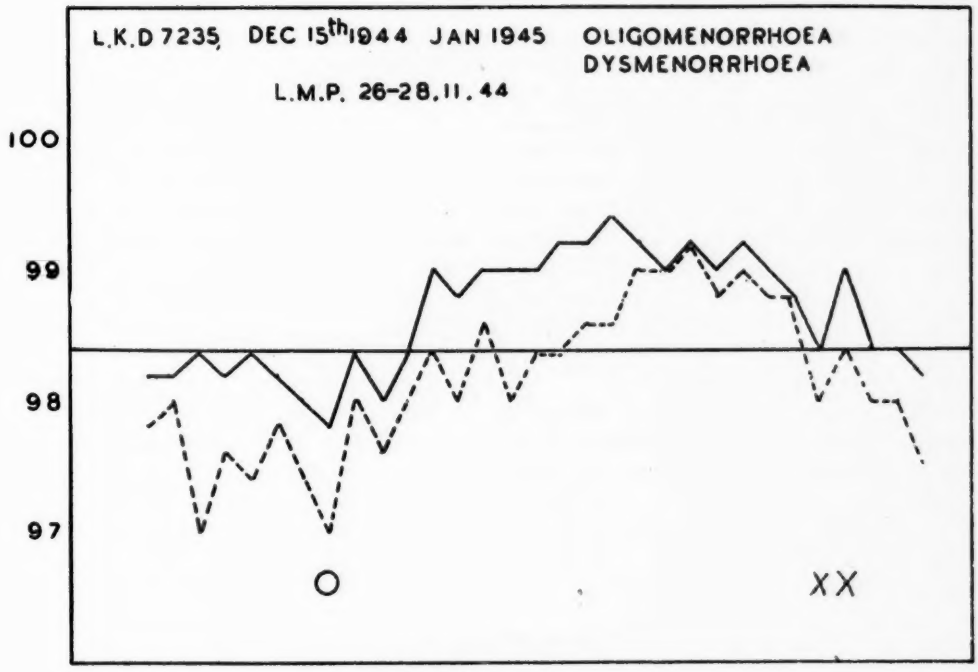
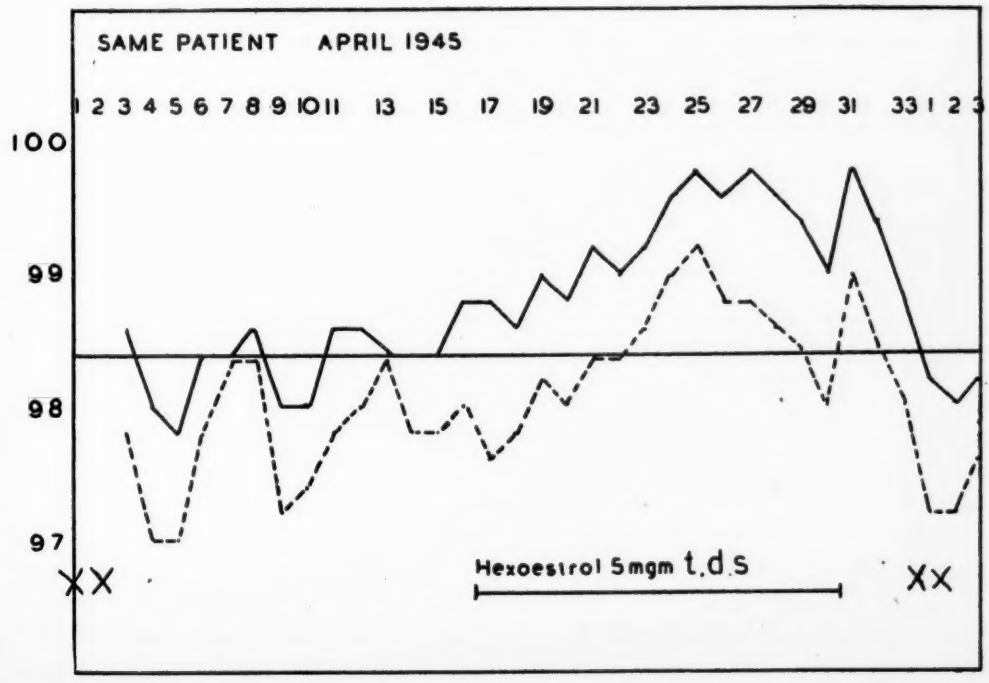

L.K.D 7235 DEC 15th 1944 JAN 1945 OLIGOMENORRHOEA
DYSMENORRHOEA
L.M.P. 26-28.11.44
100
99
98
97
O
XX

Fig.9


SAME PATIENT APRIL 1945
1 2 3 4 5 6 7 8 9 10 11 13 15 17 19 21 23 25 27 29 31 33 1 2 3
100
99
98
97
XX
Hexoestrol 5mgm t.d.s
XX

by 2°F. within 4 hours after the last injection, and remained at this level for $7\frac{1}{2}$ hours (Fig. 21).

Progesterone 2 c.cm. (2 mg.) intramuscularly stopped the beginning rise of temperature and kept it at a low level for a further 3 hours, probably by protecting oestrogen against its inactivation, Pincus and Zahl.[7] The temperature then returned to the pre-injection level, proceeding however, with marked fluctuations (Fig. 22).

Progestogen Administration.

Administration of ethynil testosterone in the dosage of 60 mg. daily sublingually for 5 days to patients suffering from secondary amenorrhoea due to protracted follicular activity (either hypo- or poly-follicular) causes constantly a marked even rise of temperature and onset of bleeding about 2 days after cessation of treatment (Figs. 11, 22 and 23).

If progestogen is given together with oestrogens as, for instance, Lutocyclin 15 mg. with oestradiol benzoate 25,000 I.B.U. in one syringe intramuscularly in 3 doses on alternate days, it causes only very slight increase of temperature followed on the 3rd or 4th day after cessation of treatment by menses of normal length and flow (Fig. 24).

Androgen Administration.

Administration of testosterone propionate or methyl testosterone in small doses expresses itself in a decrease of temperature if given during the follicular phase (Figs. 14 and 15). This is in accord with the findings of Selye and others[8] that androgens in small doses have folliculoid activity. The

Fig.10

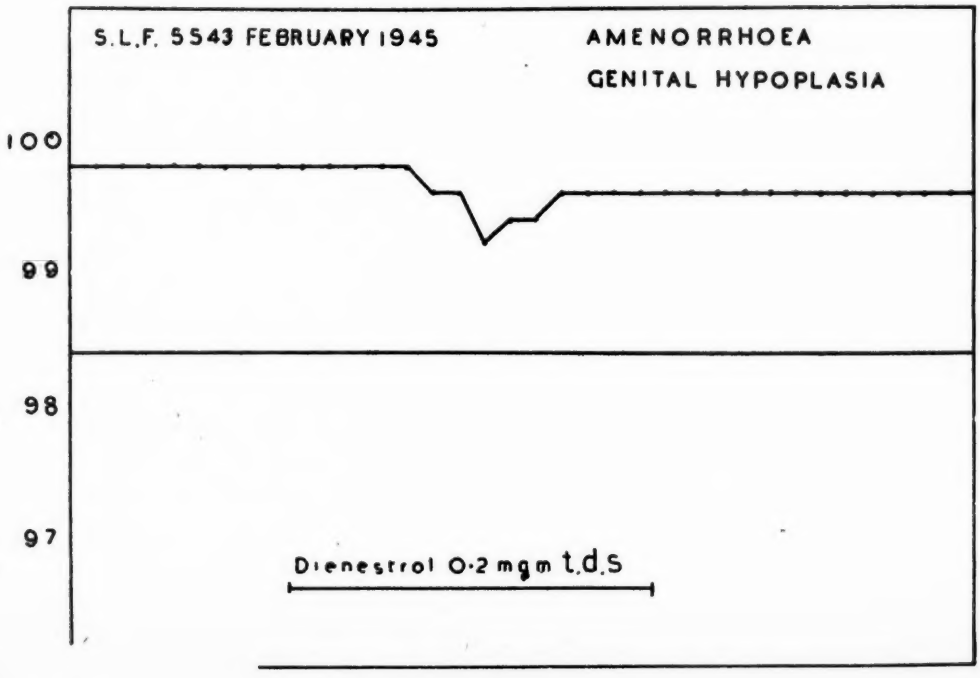


Fig.11

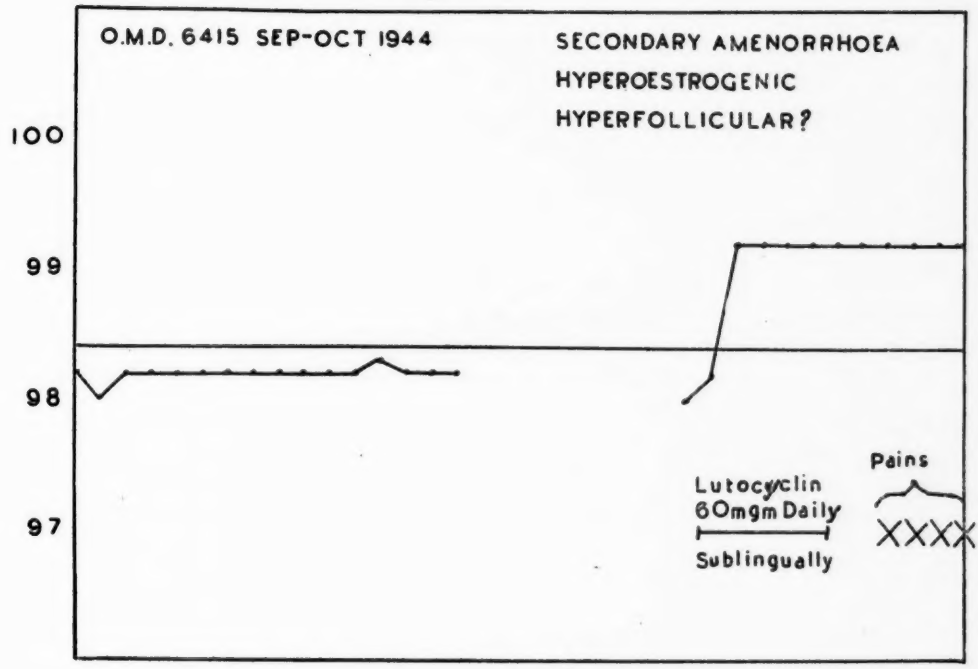

O.M.D. 6415 SEP-OCT 1944
SECONDARY AMENORRHOEA
HYPEROESTROGENIC
HYPERFOLLICULAR?
100
99
98
97
Pains
Lutocyclin
60mgm Daily
Sublingually
XXXX

Fig.12

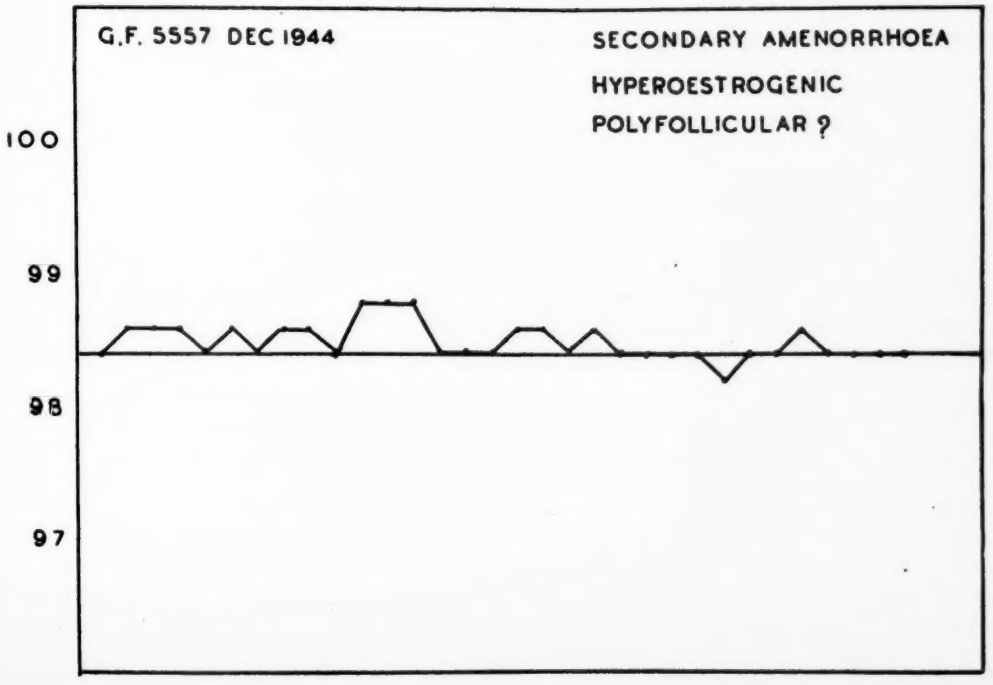
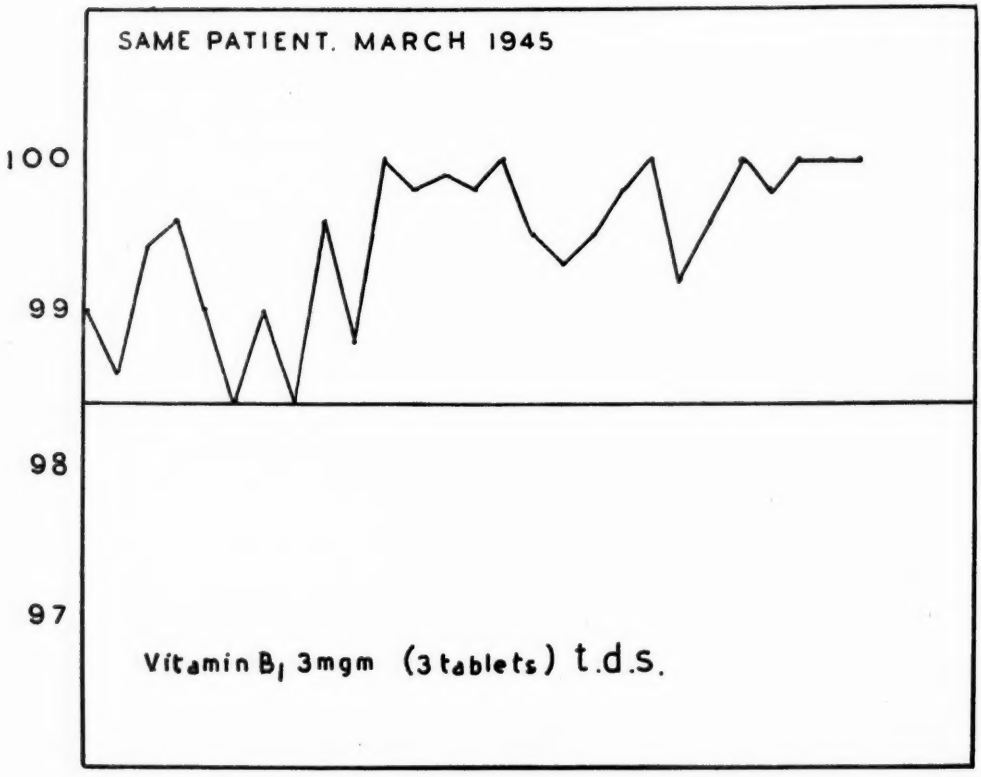

G.F. 5557 DEC 1944
SECONDARY AMENORRHOEA
HYPEROESTROGENIC
POLYFOLLICULAR ?
100
99
98
97

Fig.13



beneficial effects of androgens in the treatment of menorrhagia, metrorrhagia and polymenorrhoea may be due, not to its constricting effect of the myometrial spiral arterioles as hitherto believed, but to its folliculoid action.

Vitamin B Administration.

Vitamin B administration to patients with high oestrogenic level due to protracted follicular activity causes a marked increase of temperature (Figs. 12 and 13). This fact is in accord with Biskind and others[9] who found that vitamin B increased the inactivation of oestrogen in the liver.

DISCUSSION.

The temperature variations during the menstrual cycle closely correspond to changes in glandular activity, particularly of the pituitary gonadotrophic, follicular and luteal hormones. It is suggested that the decrease of temperature is an expression of oestrogen activity, whereas temperature rise is caused by the corpus luteum hormone.

Premenstrual Phase.

The fall of temperature during the premenstrual phase is due to corpus luteum

Fig.14

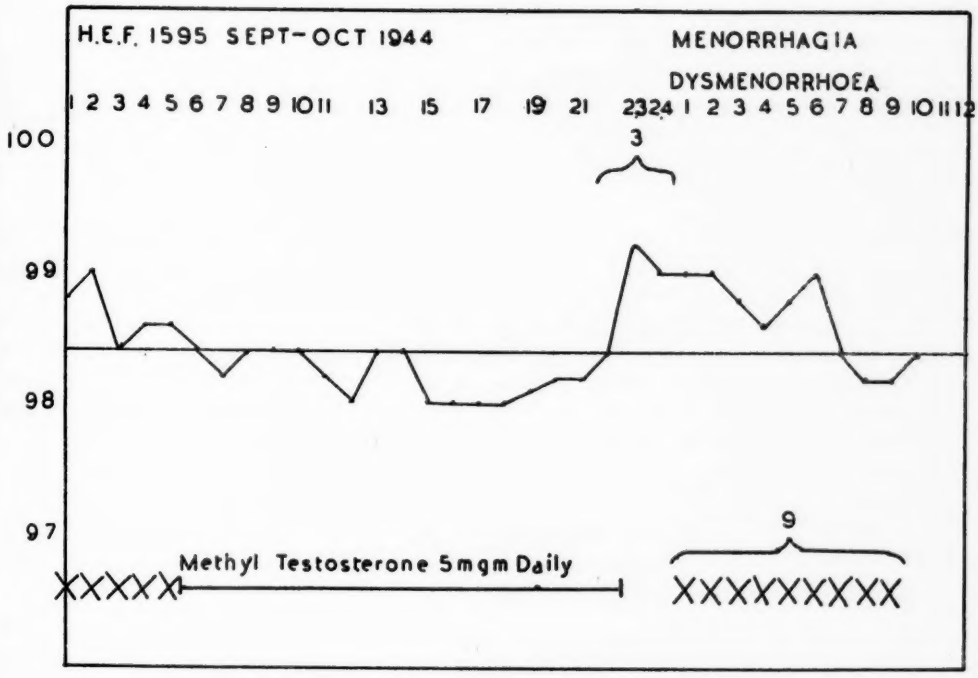
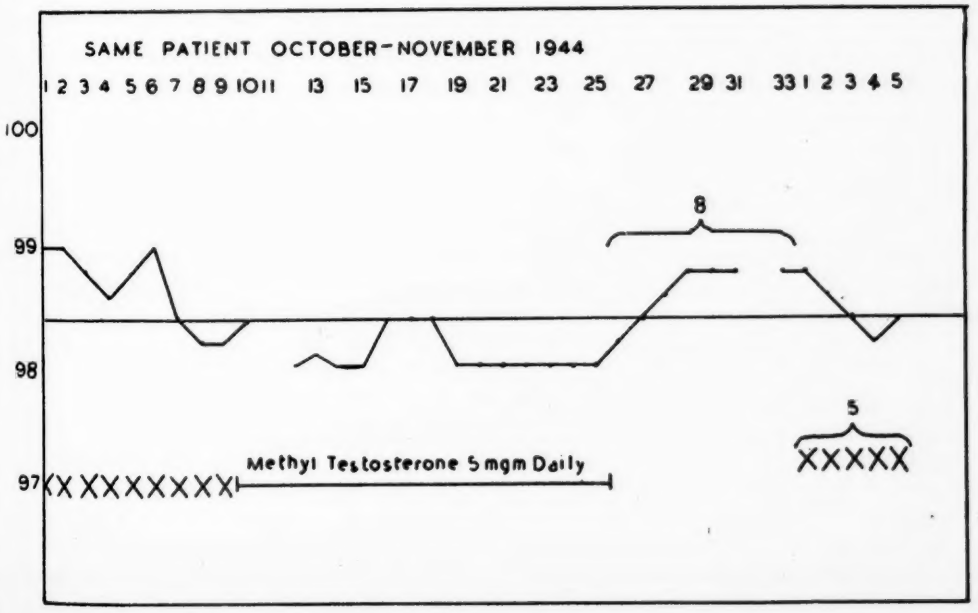

H.E.F. 1595 SEPT-OCT 1944
MENORRHAGIA
DYSMENORRHOEA
1 2 3 4 5 6 7 8 9 10 11 13 15 17 19 21 23 24 1 2 3 4 5 6 7 8 9 10 11 12
100
99
98
97
3
9
Methyl Testosterone 5 mgm Daily
XXXXX
XXXXXXXXX

Fig.15


SAME PATIENT OCTOBER-NOVEMBER 1944
1 2 3 4 5 6 7 8 9 10 11 13 15 17 19 21 23 25 27 29 31 33 1 2 3 4 5
100
99
98
97
8
5
Methyl Testosterone 5 mgm Daily
XXXXXXXXX
XXXXX

regression and renewed oestrogen excretion.

Oestrogenic activity is preceded by oestrogen and progestin withdrawal and coincides with the release of follicle-stimulating hormone of the anterior pituitary and formation of new follicles.

Menstrual Phase.

During the menstrual phase the temperature continues to decrease, owing to the still very vigorous release of F.S.H. which causes a high rate of follicle maturation. Increased oestrogenic activity inhibits the excretion of F.S.H. from the pituitary and decreases the rate of follicle maturation, which results in a diminished oestrogen excretion. This corresponds to the subsequent rise of temperature during the menstrual phase.

Follicular Phase.

The sustained low fluctuating temperature during the follicular phase corresponds to a more or less even rate of follicle maturation and oestrogen excretion.

Ovulatory Phase.

Usually, on the 14th day before menstruation, oestrogen excretion reaches its highest peak causing the sudden drop in temperature. This is followed by vigorous release of luteinizing hormone from the anterior pituitary which produces ovulation and corpus luteum formation with increased progestin excretion.

Luteal Phase.

At this stage the temperature rises to a level between 99°F. and 100°F. or more,

Fig.16

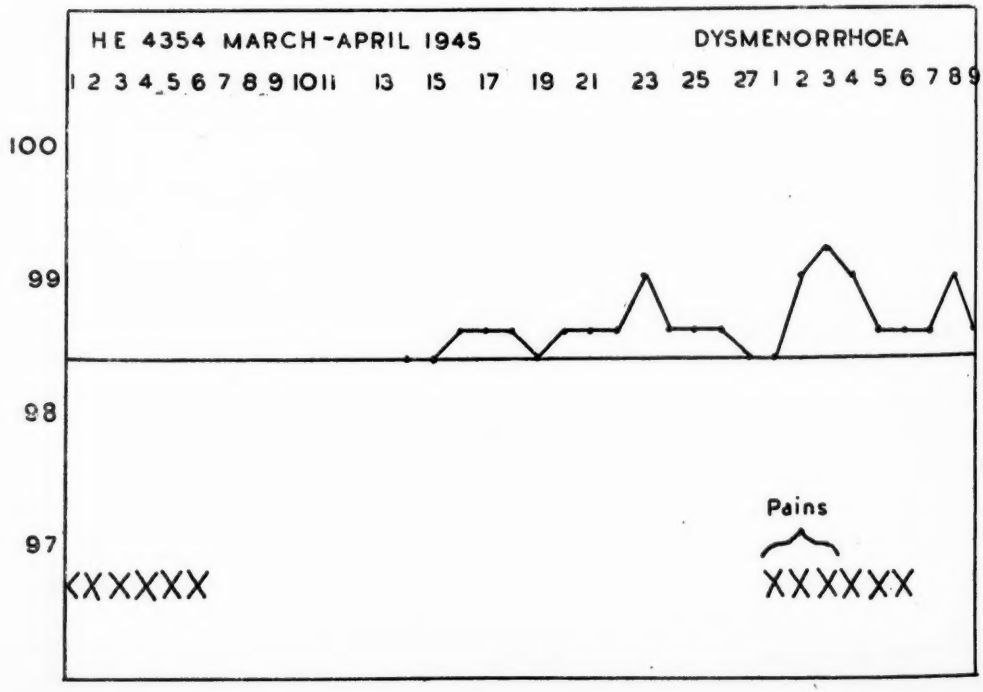
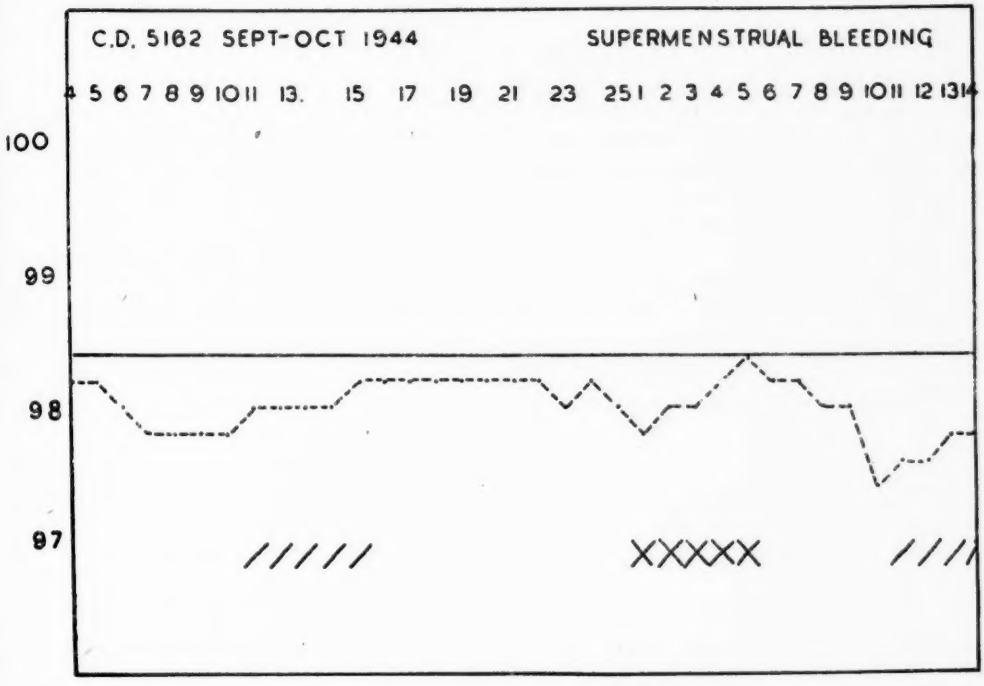


Fig.17



and remains at this level with slight fluctuations throughout the whole luteal phase. It declines 1 or 2 days before onset of menses.

Mid-luteal Phase.

The slight decrease of temperature is caused by the oestrogenic peak occurring at this stage of the phase.

The difference between the lowest temperature in the follicular phase and the highest temperature in the luteal phase is, in the normal woman, approximately 1.4°F. It is interesting to note that this difference is less obvious with the increased grade of genital hypoplasia (Fig. 3).

Secondary Amenorrhoea.

Two kinds of secondary amenorrhoea have been included in the classification of temperature curves, one characterized by persistently low temperature, and the other associated with a higher temperature curve (Figs. 10, 11 and 12).

The patients presenting a low curve showed normal genital development frequently associated with a tendency to obesity. Neither protracted nor cyclic oestrogenic treatment is of any avail in producing oestrogen withdrawal bleeding in these patients.

In the author's experience ethynil testosterone 60 mg. sublingually daily for 5 days always produced bleeding on the 2nd or 3rd day after cessation of treatment in patients suffering from hyper-oestrogenic amenorrhoea due to protracted hyper- or poly-follicular activity (Figs. 11 and 23). Such patients who, in addition, suffered

from obesity showed a loss of weight under continued treatment. Progestogen administration to these patients is always accompanied by a rise of temperature.

The persistent state of amenorrhoea in untreated patients with a high oestrogenic level may be due to the fact that the hormone is constantly above the endometrial sub-threshold bleeding point, and adequate to maintain the proliferated mucosa without causing endometrial breakdown and bleeding.

It is doubtful whether an upper bleeding threshold exists in view of the fact that most cases of amenorrhoea treated by oestrogen withdrawal showed by their vaginal temperature curves, either signs of pituitary or direct[10] ovarian stimulation (Figs. 10, 20, 25, 26, 27 and 28), or sub-threshold oestrogen withdrawal bleeding (Figs. 9, 25 and 27).

It seems more justifiable to speak of menses accompanied by a high oestrogenic level as in the case of normal menses which, although preceded by oestrogen withdrawal, is usually associated with a high oestrogenic level.

Low oestrogenic bleeding, on the other hand, occurs in cases of menorrhagia, metrorrhagia and intermenstrual bleeding (Figs. 14, 15, 16 and 24), is usually of protracted nature and is easily suppressed by

Fig.18

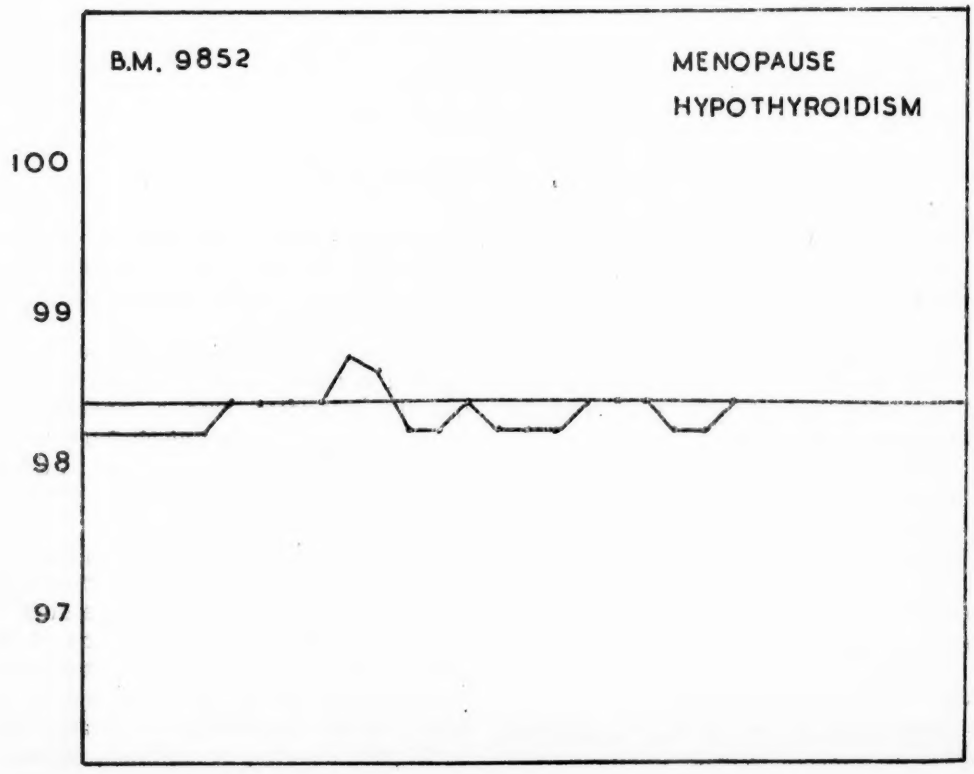
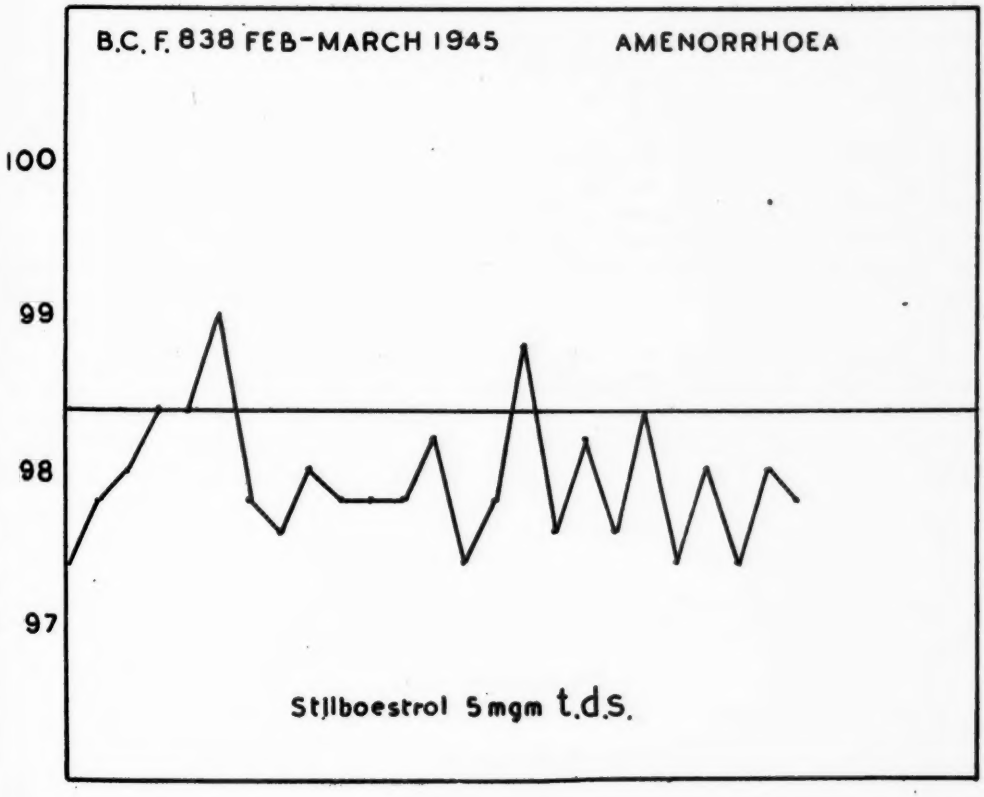


Fig.19



raising the oestrogenic level. One injection of oestradiol benzoate 100,000 I.B.U. intramuscularly usually stops bleeding within 24 hours.

A low constant temperature curve seems to be associated with hyperfollicular amenorrhoea, whereas the low curve with slight fluctuations may be a sign of polyfollicular amenorrhoea. The latter is usually of shorter duration (Fig. 12).

The constant high temperature curve denoting oestrogen deficiency is usually found in patients with signs of genital hypoplasia (Fig. 10).

In cases of a vaginal evening temperature curve above the level of 98.8°F. (Fig. 29) the treatment of choice is cyclic oestrogen-progestogen administration (Fig. 7).

At values below 98.8°F. denoting a somewhat higher oestrogenic level sole oestrogen withdrawal treatment may suffice (Figs. 27, 28 and 29).

As the oestrogenic level increases the administration of the hormone may remain without effect, and the treatment of choice in these cases is progesterone 15 mg., and oestradiol benzoate 25,000 I.B.U. in one syringe intramuscularly alternate days in 3 doses. Menses of normal length and flow usually follow on the 3rd or 4th day after cessation of treatment (Figs. 29 and 24).

Still higher levels of oestrogen require only progestogen treatment in the form of ethynil testosterone 60 mg. sublingually daily for 5 days or progesterone 15 mg. intramuscularly for 3 days (Figs. 11 and 23).

An initial success may sometimes be obtained with progestogen at high temperature levels, while subsequent administration acting on a previously reduced oestrogenic level will remain without results.

The temperature values are only approximate and should be regarded as such when, in accordance with temperature level, the particular treatment is decided upon.

Oligomenorrhoea.

Infrequent bleeding from a secretory type of endometrium has revealed temperature graphs showing a variable prolonged follicular phase with a fairly constant luteal phase. Menses occurs 14 days or more after ovulation (Fig. 8).

There is as yet no evidence at hand why ovulation is delayed in these cases.

Repeated observations made on the basis of endometrial biopsies are conflicting as to whether oligomenorrhoea is caused by a prolonged follicular phase or protracted luteal phase.

Too few cases of oligomenorrhoea have been investigated by their temperature to allow the support of one or other opinion.

Infrequent bleeding from non-progesta-

Fig.20

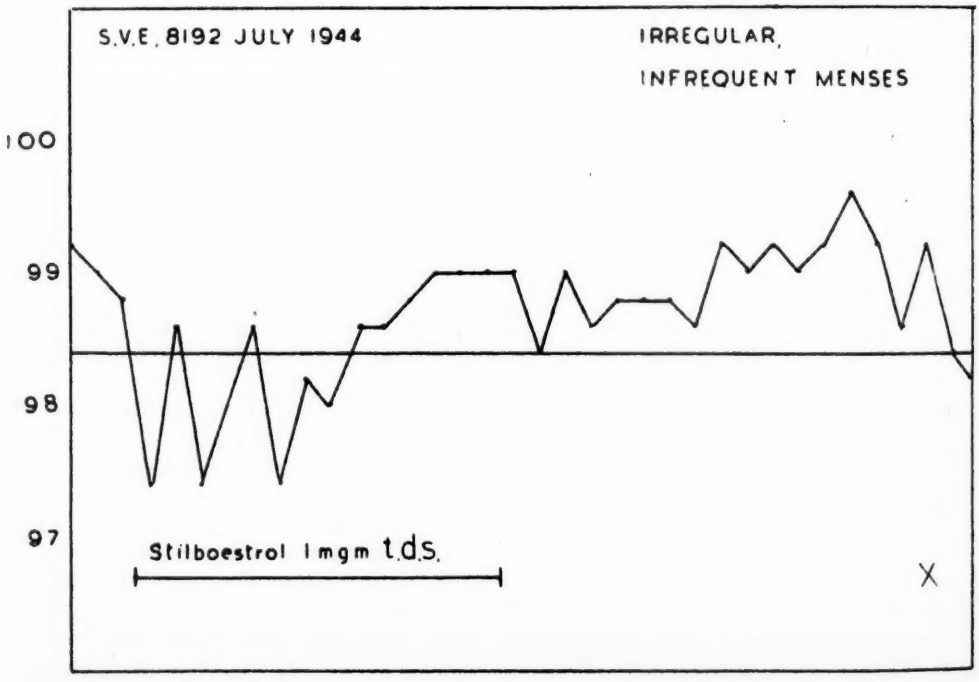
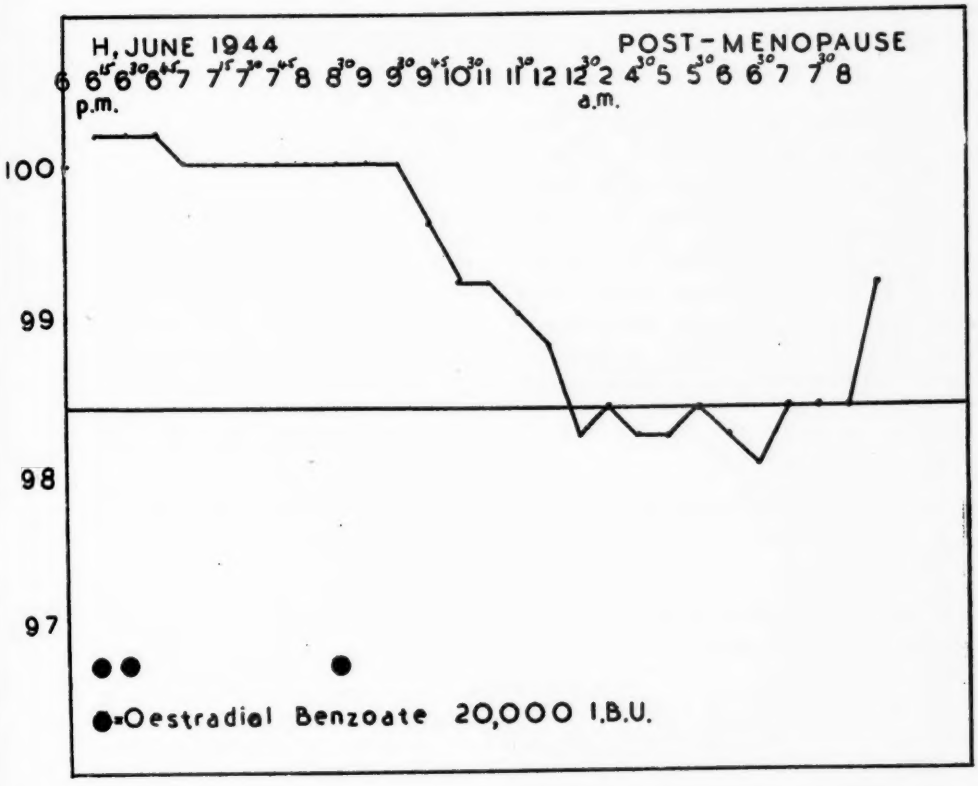


Fig.21



tional endometria is classified under secondary amenorrhoea.

Menorrhagia.

The temperature curves in cases of menorrhagia show a prolonged follicular and short luteal phase. Bleeding occurs in short distance of ovulation and is characterized by a lack of the premenstrual phase in which normally the temperature falls (Figs. 14 and 15).

During the menstrual phase the temperature remains at a high level and falls at the end or after the menstrual phase. In fact, however, the follicular and luteal phases are approximately of the same and normal length, but bleeding occurs before corpus luteum regression has taken place. This is in keeping with the observations of Traut and Kuder,[11] in whose opinion menorrhagia occurs from endometria which show evidence of deficient luteal influence. Conversion to the secretory phase occurs only in scattered areas.

Further supporting evidence is supplied by Samuels[12] who found that pregnandiol continued to be excreted after the onset of menstruation, and oestrogen and androgen values were within normal limits.

The temperature investigations so far carried out show that length and amount of bleeding are in direct relation to the stage

of the luteal phase at which endometrial breakdown takes place. The later bleeding occurs in the luteal phase, the less it is in amount and duration.

Dysmenorrhoea.

The menstrual phase in cases of dysmenorrhoea is characterized by a premenstrual rise of temperature declining during or after cessation of bleeding, which may be interpreted as protracted progestin function (Figs. 14, 15 and 16). In cases in which both vaginal and oral temperatures were taken, in addition to the premenstrual rise the oral temperature rose to the same level as the vaginal curve. The oral temperature being oestrogen-sensitive denotes, when it rises, a lack of oestrogen (Figs. 7 and 8).

It seems that in dysmenorrhoea the menstrual phase is characterized by protracted action of progestin in the absence of oestrogen activity.

This is in accordance with the experience of Hamblen[13] that oestrogens relieve dysmenorrhoea, and with the opinion of Hirst and others[14] that dysmenorrhoeic pain is of sympathetic nature and can be blocked out by antagonistic action of the parasympathetic. On the basis of Reynolds[15] observations that oestrogens have a parasympatheticomimetic action mediated by

Fig.22

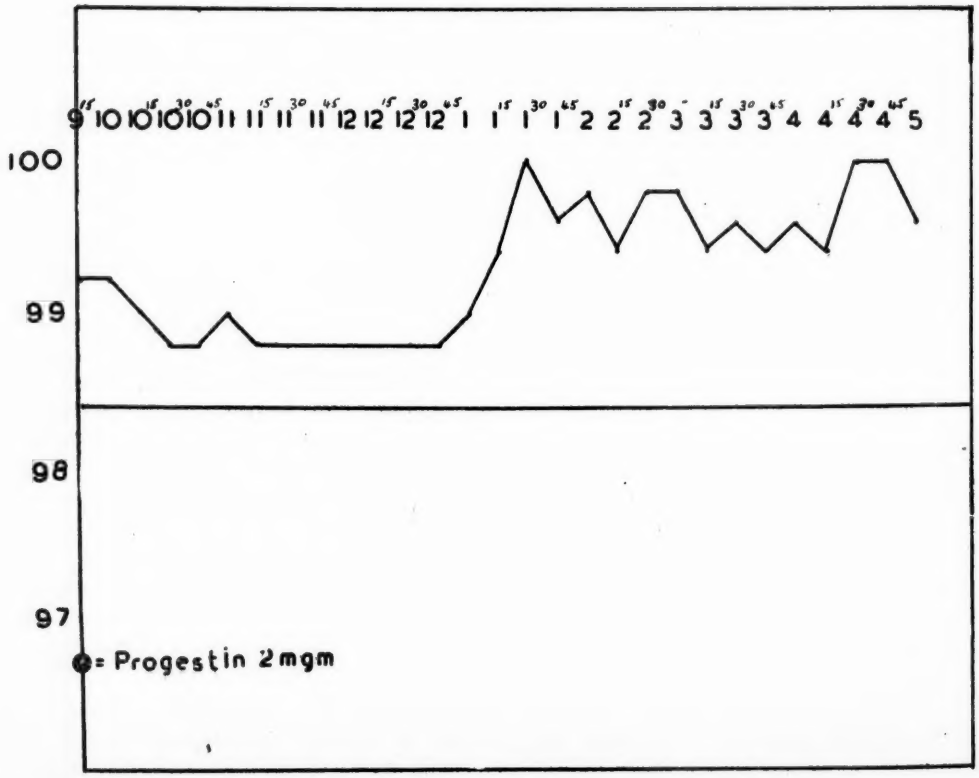


Fig.23

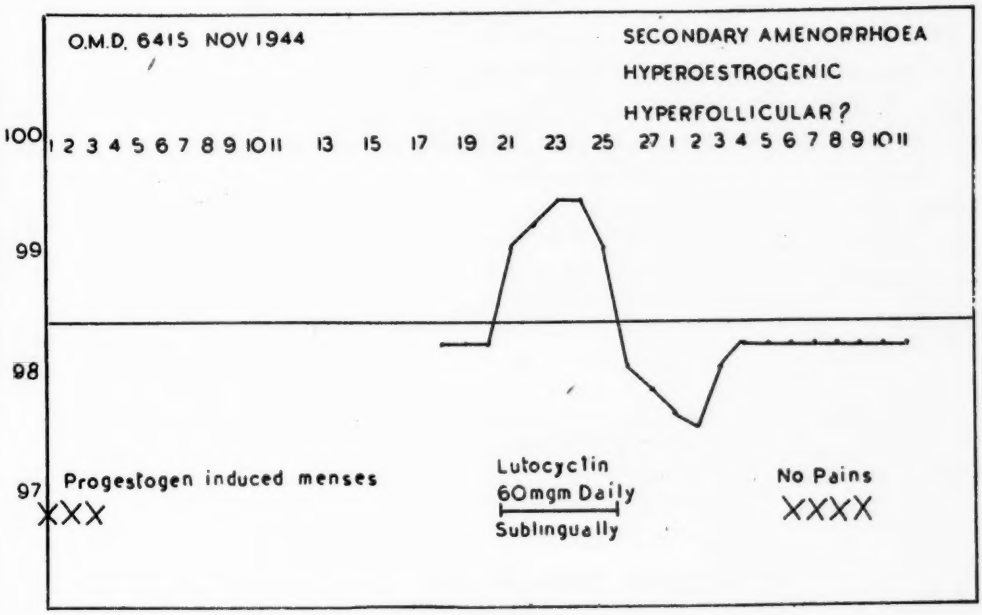

O.M.D. 6415 NOV 1944
SECONDARY AMENORRHOEA
HYPEROESTROGENIC
HYPERFOLLICULAR?
100
99
98
97
1 2 3 4 5 6 7 8 9 10 11 13 15 17 19 21 23 25 27 1 2 3 4 5 6 7 8 9 10 11
Progestogen induced menses
XXX
Lutocyclin
60mgm Daily
Sublingually
No Pains
XXXX

Fig.24

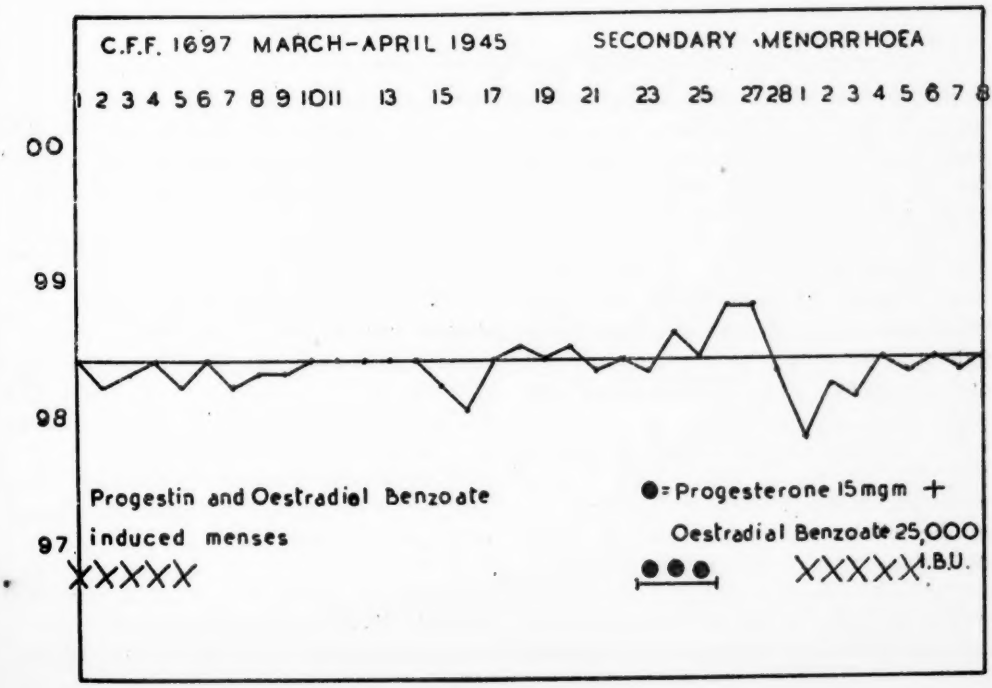
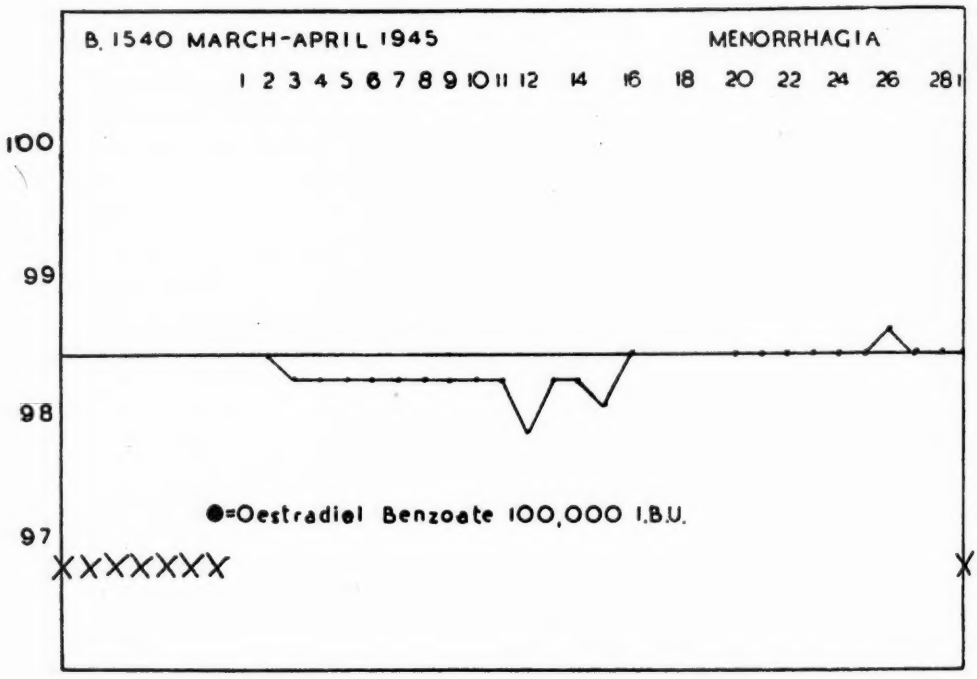

C.F.F. 1697 MARCH-APRIL 1945
SECONDARY AMENORRHOEA
1 2 3 4 5 6 7 8 9 10 11 13 15 17 19 21 23 25 27 28 1 2 3 4 5 6 7 8
00
99
98
97
Progestin and Oestradiol Benzoate
induced menses
XXXXX
●= Progesterone 15mgm +
Oestradial Benzoate 25,000
I.B.U.
●●●
XXXXX

Fig.25



an inhibition of acetylcholine esterase, they conclude that dysmenorrhoea is a functional condition brought about by a relative deficiency of oestrogen which results in over-activity of the sympathetic nervous system, characterized by the production of vasoconstriction and pain. In the author's own experience administration of ethynil testosterone in the dosage of 300 mg. over 5 days to patients suffering from amenorrhoea frequently causes dysmenorrhoeic pain.

The mechanism by which protracted progestin activity combined with lack of oestrogen causes dysmenorrhoeic pain, is, on the whole, not quite clear. A better understanding is obtained if the precipitating factor of normal bleeding with the *rôle* of the ovarian hormones is closely examined. Oestrogen dilates the endometrial blood vessels and increases their permeability,[16] preventing undue congestion. Progestin causes a decrease in tonus of the uterine muscle enhancing congestion in the endometrium.

Little tissue loss occurs in hyperplastic bleeding whereas greater tissue loss takes place from a secretory type of endometrium.[17] As functional dysmenorrhoea is almost always preceded by a secretory type of endometrium[18] dysmenorrhoea is, mathematically expressed, equal to the process normally occurring in the secretory type of endometrium prior to bleeding, plus protracted corpus luteum activity, minus oestrogenic action.

In the normal cycle during the premenstrual phase, oestrogen and progestin withdrawal takes place, endometrial activity ceases, and rapid regression and shrinkage

of the mucosa occurs. This results in a disproportion between the length of the coiled arteries and the thickness of the endometrium. With further regression of the mucosa, more coils are formed retarding the blood flow and causing stasis.[19] This precedes the flow by 1 to 3 days. Four to 24 hours before onset of bleeding, the coiled arteries become constricted at their base adjacent to the uterine musculature, and ischemic necrosis in the superficial parts of the endometrium results. Bleeding occurs by escape of blood from the capillaries and arterioles by diapedesis or through the degenerating walls.

In the dysmenorrhoeic endometrium only oestrogen withdrawal occurs while corpus luteum activity persists. This results in a delayed shrinkage and regression of the mucosa and decreased tonus due to progestin activity, which produces increased engorgement not counteracted by the action of oestrogen. The resulting tissue loss and the unusual vascular engorgement seems to be the causative factor in dysmenorrhoeic pain.

Intermenstrual Bleeding.

Intermenstrual bleeding occurs with a very slight temperature rise of usually 0.2°F. only. This takes place within a monotonous curve on a high level and of only minor fluctuations (Fig. 17). It seems that the oestrogenic level is only slightly above the endometrial bleeding threshold. Therefore, only a small decrease in the oestrogenic level is necessary to precipitate bleeding. This is in keeping

Fig.26

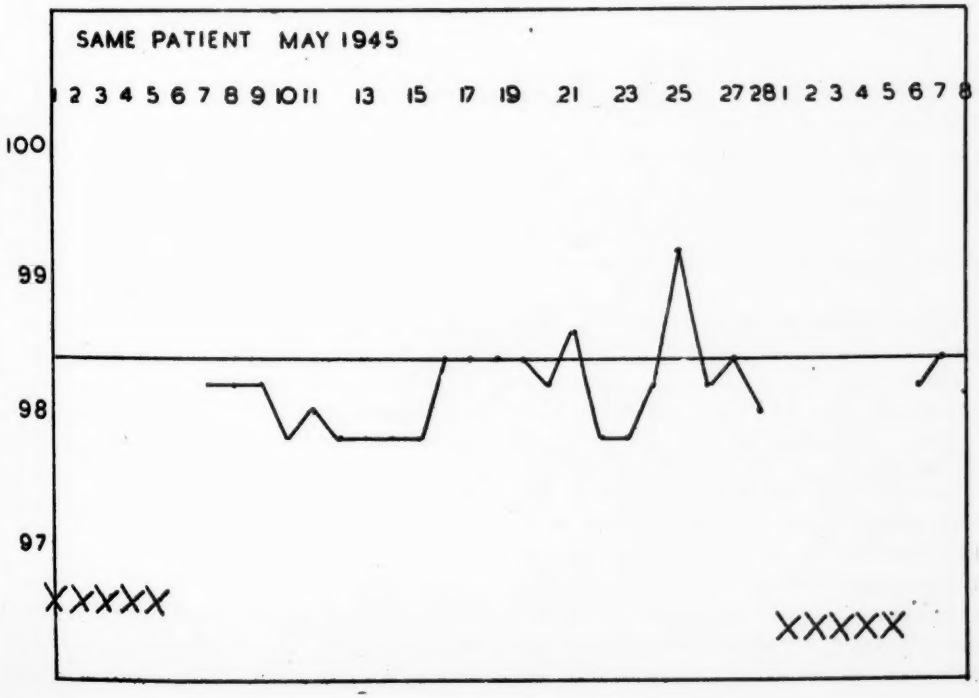
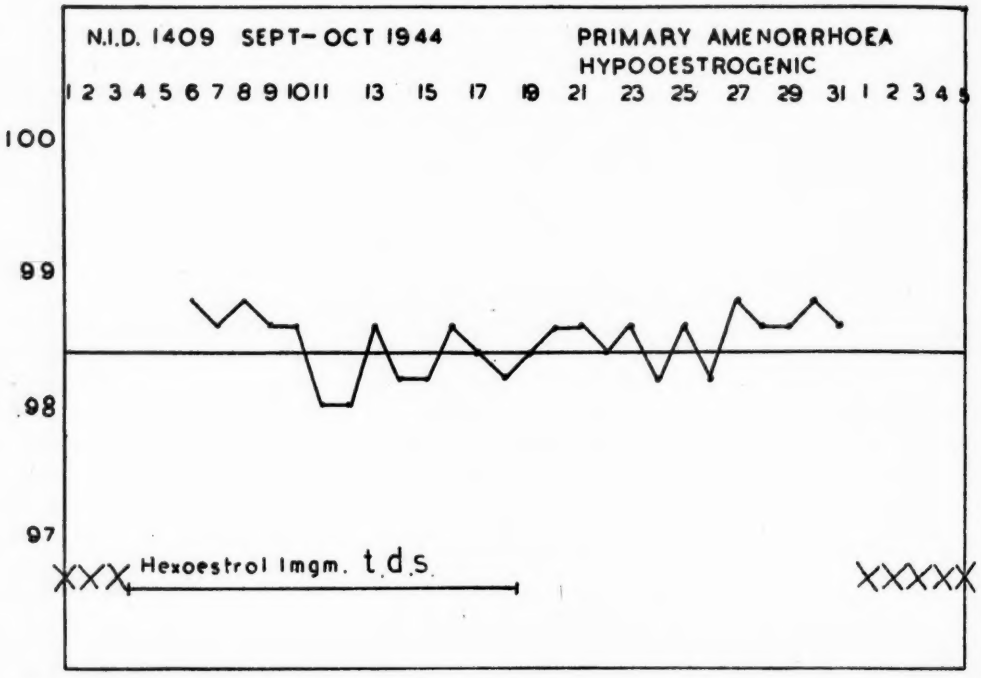


Fig.27


N.I.D. 1409 SEPT–OCT 1944
PRIMARY AMENORRHOEA
HYPOOESTROGENIC
1 2 3 4 5 6 7 8 9 10 11 13 15 17 18 21 23 25 27 29 31 1 2 3 4 5
100
99
98
97
Hexoestrol 1mgm. t.d.s.

with Zuckerman's[20] observations that castrate monkeys receiving oestrogen in doses from 850 to 3000 I.U. daily did not bleed when the dose was reduced to 200 I.U. but a reduction to 150 I.U. was followed by bleeding of all monkeys within a few days.

Oestrogen, Progestogen, Androgen and Vitamin B Administration.

The observation of patients by temperature graphs has proved a valuable aid in diagnosing the effects of hormone treatment on the glands of reproduction. Furthermore, the study of temperature curves aids in deciding on the kind of hormone to be administered and its approximate dosage. A clear reflection of oestrogenic effects occurs in cases of amenorrhoea. It appears that oestrogen withdrawal bleeding is not as Novak[21] stated: "to push the pendulum of the rundown menstrual clock for a single idle incomplete beat when what we need is something to wind the clock" but causes, in many cases, stimulatinon to the pituitary gland (Figs. 10, 25, 28).[22]

In fact, Eskin[23] demonstrated that injection of oestradiol benzoate into immature rats produced a release of gonadotrophic hormone from the anterior pituitary gland. The pituitary glands of the treated and controlled animals were examined, showing those of the treated animals to contain much less gonadotrophic substance than those of the untreated animals. The injections of oestradiol benzoate were followed by the formation of corpora lutea.

Oestrogen lowers temperature. However, graphs of patients under cyclic oestrogen treatment show frequently a sudden rise of temperature which starts during

oestrogen administration, maintaining a high level during the luteal phase, and is followed by menstruation (Figs. 20 and 28).

It is, furthermore, in keeping with the clinical evidence that amenorrhoeic patients who have undergone a 3 to 6 months course of oestrogen withdrawal bleeding, continue to bleed at regular intervals after cessation of treatment.

In one case the administration of ethynil testosterone 60 mg. daily for 5 days apparently stimulated increased release of F.S.H. from the anterior pituitary lobe (Fig. 23).

That progestin exerts a stimulating effect on the anterior pituitary has recently been demonstrated by Eskin[24] showing in the rabbit increased gonadotrophic activity following coitus after one injection of 0.5 Rabbit Units of progestin. Haemorrhagic follicles, rarely occurring after normal coitus, were observed in rabbits treated with progestin prior to copulation.

There is a difference between the curve of morning and evening temperatures in reference to level, fluctuations and distance between the oral and vaginal curves. Particularly marked is the difference in those patients who are given treatment which elicits temperature changes (Fig. 4).

At the present stage of knowledge it is suggested that preferably evening temperatures are used for the investigation of cyclic changes in the woman. The taking of temperature in the morning is for many women inconvenient and frequently omitted in the early morning rush. In fact, most patients prefer to take their temperature in the evening.

The therapeutic effects are better reflected in the combined oral and vaginal

Fig.28

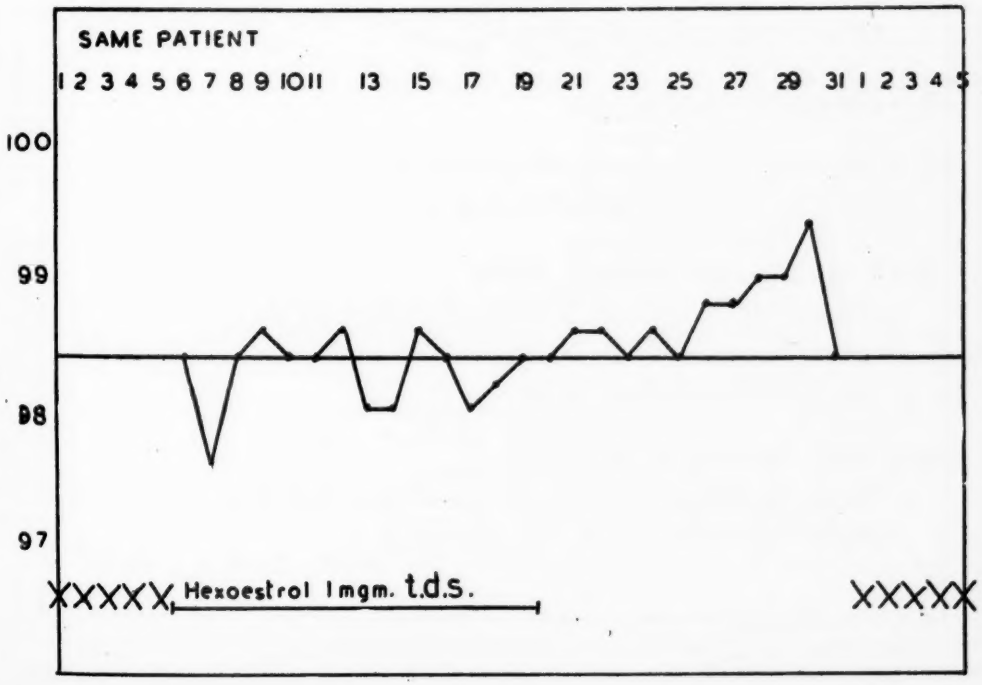
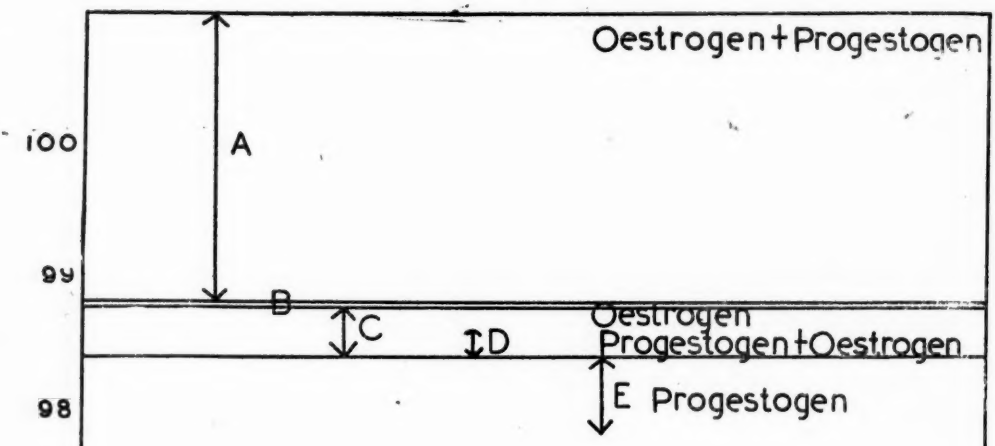


Fig.29



A = Severe oestrogen deficiency below bleeding threshold. Treatment = Cyclic oestrogen + progestogen

B = Bleeding threshold

C = Low oestrogenic level above bleeding threshold.
Treatment = Cyclic oestrogen

D = Medium oestrogenic level.
Treatment = Progesterone 15mgm + oestradiol benzoate 25,000 I.B.U. intramuscular in 3 doses on successive days.

E = High oestrogenic level.
Treatment = Ethynil testosterone 60mgm sublingually daily for 5 days.

evening temperature graphs. However, for the investigation of general cyclic events in patients receiving treatment which may elicit temperature changes, the combined curves show a more regular pattern if recorded according to morning temperatures.

Summary.

The vaginal and oral, or both temperatures taken simultaneously, were investigated in 41 women over 150 cycles.

The normal cycle shows a clear differentiation of its various phases, including ovulation.

In amenorrhoea, oligomenorrhoea, menorrhagia, dysmenorrhoea and intermenstrual bleeding, the temperature curves are of great diagnostic value. Special significance is attributed to the changing relation of oral and vaginal temperature in dysmenorrhoea.

In the therapy of menstrual disorders the temperature curve aids in deciding on the hormone and dosage to be administered, and indicates its degree of effectiveness.

The unmistakable sign of ovulation is of importance in cases of subfertility as well as for birth control owing to the easily recognizable safe and unsafe periods.

No objections have been encountered from patients who were asked to take their vaginal or oral temperature, or both simultaneously for many cycles.

Acknowledgment.

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The Association of Erythroblastosis Foetalis and Accidental Antepartum Haemorrhage

BY

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ERYTHROBLASTOSIS foetalis, which develops most commonly when anti-Rh agglutinins is produced in an Rh negative woman by an antigen entering her circulation from her Rh positive foetus[1, 2, 3, 4] has received much attention in the past 3 years.

Fifteen per cent of white persons are Rh negative and 12 per cent of marriages are between Rh negative women and Rh positive men, but the incidence of erythroblastosis is found by Potter, Davidsohn and Crunden[5] at the Chicago Lying-in Hospital to be only 1 in 1,000 births. They thought that this disproportionately low incidence might be due to: (1) Childless or 1 child marriages; (2) variable potency of the Rh antigen of the infant in producing agglutinins in the maternal blood; (3) variable ability of the placenta to prevent the passage of the antigen; (4) variable maternal response to the introduction of the Rh antigen into the bloodstream; (5) variable ability of the placenta to prevent the passage of the agglutinins.

As regards the first point, Hogben[6] states "that it is certain in the light of statistics already to hand that second or later born heterozygous offspring of Rh negative mothers by Rh positive fathers are far more numerous than recognizable cases of neonatal haemolytic anaemia and associated miscarriages or stillbirths."

Boorman, Dodd and Mollison[3] noted the failure of correspondence between titre of agglutinins and severity of the disease, so that variable potency in the Rh antigen in the infant (unless the antigen has been introduced by previous transfusion of the mother with Rh positive blood), variable maternal response, and variable permeability of the placenta for antigen and agglutinins are the important factors.

The mode of passage of the Rh antigen, thought to be confined to the red cells, across the placenta has puzzled everyone, and Lubinski, Benjamin and Strean[7] considered it impossible unless some pathological conditions were present. Javert[8] found haematomas in the intervillous spaces in 8 out of 35 placentae from cases of haemolytic anaemia of the newborn.

In 2 out of 3 cases of erythroblastosis occurring in 6 months (April to September 1944) at Queen Charlotte's Hospital, there was premature separation of the normally implanted placenta with antepartum haemorrhage. As both these mothers had previously borne only healthy children, it seemed possible that the haemorrhage from the placental site with rupture of the maternal sinuses and consequent damage to the placenta might be the factor allowing transmission of antigen and agglutinins. As both conditions (i.e. premature separation of placenta and erythroblastosis) are comparatively rare, although the number of cases was small, these facts suggested that the association might be of some significance.

A careful study of the literature revealed

little. Schwartz and Levine[9] had found some association between the two conditions. In 1937 a woman transfused for intra- and postpartum haemorrhage at the delivery of a macerated foetus, had a severe reaction after transfusion with her husband's blood. She was found to be Rh negative and her husband Rh positive. They also found that in 4 cases of stillbirth associated with premature separation of the normally implanted placenta, 2 were due to erythroblastosis, but concluded that the foetal death almost certainly antedated the premature placental separation, and suggested that "although most cases of premature separation of the normally implanted placenta do not appear to be accompanied by erythroblastosis," analysis of a longer series was indicated.

Accordingly, with the help of Dr. Allott of Lewisham Group Laboratory, all cases of antepartum haemorrhage occurring at St. Alfege's Hospital, between February and June 1945, were investigated with the following results:

1. Placenta praevia: 6 cases.
   Rh reports are available in only 5 of these, and all were positive.
   (Genotypes in 4 where they were determined, were Rh_2rh, Rh_1Rh_2, Rh_2rh, Rh'rh.)
2. Accidental antepartum haemorrhage, mother Rh negative, father Rh positive;* 5 cases.
3. Accidental antepartum haemorrhage, mother Rh positive; 5 cases.
4. Antepartum haemorrhage, placental insertion not determined, mother Rh positive: 1 case.
5. Accidental antepartum haemorrhage, mother and father both Rh negative: 1 case.

The tables give details of the pregnancies in groups 2 to 5, and of the 2 cases from Queen Charlotte's Hospital (*vide supra.*)

The series is small and the full scope of the blood investigations necessary is only now being realized, as with Cases 3a and b, so that a great deal more work is necessary. Later Dr. Allott and I hope to publish a report on this work.

In the meantime, the following facts emerge from the St. Alfege's series of cases. Five out of 10 (50 per cent) of the mothers who had an accidental antepartum haemorrhage were Rh negative with Rh positive husbands* and 3 of these had anti-Rh agglutinins. Of the 3 who were delivered soon after the antepartum haemorrhage, 1 had a child with only a moderate degree of jaundice, who recovered without transfusion, another a child with very gross hydrops, and the 3rd a child stillborn, possibly as a result of the course of labour. In the 2 mothers who were not delivered until some weeks after the first haemorrhage, the foetus was stillborn, macerated, and of a size corresponding roughly with death at the time of onset of the bleeding. Of the cases with Rh positive mothers, in only 2 were Rh genotypes determined; the mothers were found to be Rh_2rh and Rh_1rh, with children Rh_1Rh_2 in each case. This could theoretically make possible the development of the less common Γ and H antibodies in the 2 mothers, but evidence of their presence was not found.

It is too early to dogmatize, but it would seem justifiable to conclude that the woman in whom iso-immunization can occur, is abnormally prone to accidental antepartum haemorrhage, and the ensuing placental damage may be a factor in transmission of antigen and agglutinin. There seems, except in case 2d, to be an association between the time between delivery and bleeding and the severity of the erythroblastosis and titre of the agglutinins.

* Except the husband of Case 2g, who cannot be tested.

TABLE OF CASES.

D

	Mother's blood and anti Rh agglutinins	Father	Other children	Fate of pregnancy	Notes on pregnancy and labour
	(2) *Accidental Antepartum Haemorrhage in Rh negative Mothers.* (*Queen Charlotte's Hospital*).				
2a.	Group A. Rh negative. Doubtful	Rh + ve	(1) Died age 3½ months 1934 (2) 3 months miscarriage 1935 (3) Alive and well 1936 (4) Alive and well (Toxaemia of pregnancy) 1939	Live male infant, 3¾ pounds. Developed jaundice, splenomegaly and hepatomegaly. Recovered. Group O Rh + ve.	Brisk haemorrhage at 32/52. Artificial rupture of membranes; placenta not felt. Spontaneous delivery 10 hours after first haemorrhage.
2b.	Rh negative. Unknown	Unknown	(1) Alive and well 1942	Live female infant, 2¾ pounds. Developed jaundice and haemolytic anaemia. Recovered. Rh + ve.	Slight to moderate continuous loss from 17 hours before onset of labour until delivery at 30/52. Placenta not felt. Spontaneous delivery 24 hours after first haemorrhage.
	(2) *Accidental Antepartum Haemorrhage in Rh negative Mothers.* (*Saint Alfege's Hospital*).				
2c.	Group O. Rh negative. 10 days antepartum incomplete antibody in 1/64 dilution: 7 days in 1/128 dil:	Group B. Rh_1 Rh_1	(1) Twins (a) stillborn (b) alive and well Rh_1,rh 1936 (2) Stillborn 1939 (3) Stillborn 1941	Macerated foetus about 26/52	Irregular scanty haemorrhage from about 24/52. Movements not felt from 26/52. Further haemorrhages in hospital 4 and 6 days before delivery. Repeated medical inductions resulted in spontaneous delivery 40/52 after last period.
2d.	Group A. Rh negative. Very doubtful	Rh + ve	(1) Alive and well Rh + ve 1940 (2) Alive and well Rh + ve 1942 (3) Stillborn 1943	Macerated foetus about 26/52	Four moderately severe haemorrhages from 30/52, movements ceasing after the first. Foetal heart not heard on admission. Repeated medical inductions given. Delivery complicated by further haemorrhage and severe postpartum haemorrhage requiring transfusion.
2e.	Group A. Rh negative. None detected	Rh + ve	(1) Alive and well 1942 (Not available for testing)	Live male infant 4¼ pounds. Slight jaundice in early days; slow in gaining weight. Rh + ve.	Moderately severe antepartum haemorrhage at 34/52 followed by onset of labour. Artificial rupture of membranes; os over half dilated; placental edge just felt in lower segment. Spontaneous delivery 22 hours after first haemorrhage.
2f.	Group O. Rh negative. 1st day p-p doubtful, 4th day p-p in 1/64 dil: 20th day p-p in 1/256 dil:	Rh_1 Rh_2	(1) Alive and well 1935 (2) Alive and well Rh_1 rh 1937 (3) Stillborn—premature 1938 (4) Alive and well Rh_2 rh 1942	Very gross hydrops foetalis. Lived a few minutes only.	Admitted as hydramnios. X-ray suggested hydrops. During the night developed severe antepartum haemorrhage. Caesarean section performed. Placenta inserted in upper segment.
2g.	Group O. rh rh. None 2 months after delivery	Not available	(1) Alive and well 1942	Stillborn. P.M. showed asphyxia.	First seen at term with antepartum haemorrhage, not in labour. Artificial rupture of membranes. Placenta not felt. Very strong pains. Reposition of prolapse of both arms was necessary.

TABLE OF CASES.

	Mother's blood	and anti Rh agglutinins	Father	Other children		Fate of pregnancy	Notes on pregnancy and labour
		(3) *Accidental Antepartum Haemorrhage in Rh positive Mothers.* (*Saint Alfege's Hospital*).					
3a.	Group O. Rh_1 rh		Unobtainable	(Primigravida)		Live female infant, $4\frac{1}{2}$ pounds. Slow in gaining weight. Group O, Rh_1 Rh_2	34/52 admitted with very severe antepartum haemorrhage. Caesarean section performed—much haemorrhage into uterine muscle. Placenta in upper uterine segment.
3b.	Group B. Rh_2 rh		Unobtainable	(1) Alive and well	1942	Live female infant, 6 pounds Group O, Rh_1 Rh_2	Slight loss just before onset of labour, increasing after rupture of membranes and becoming profuse as head appeared at vulva. Forceps delivery. Point of rupture of membranes 4 inches from placental edge.
3c.	Group O. Rh + ve	None	Unobtainable	(1) Alive and well	1941	Live infant, $8\frac{1}{2}$ pounds.	Small bright red loss before admission at 30/52. Discharged herself against advice. Spontaneous delivery at 40/52.
3d.	Group O. Rh + ve	None	Unobtainable	(1) Alive and well	1937	Live infant, $7\frac{1}{4}$ pounds.	Bright red loss at 32/52. Examined at 36/52. Placenta not felt. Spontaneous delivery at 38/52.
3e.	Group A. Rh + ve	None	Unobtainable	(Primigravida)		Live male infant, 8 pounds.	Very slight haemorrhage at 34/52. Blood pressure 150/110; slight albuminuria. Toxaemia resolved very rapidly. Examined at 36/52. Placenta not felt. Normal delivery at 40/52.
		(4) *Antepartum Haemorrhage—Placental Insertion not Determined.* (*Saint Alfege's Hospital*).					
4.	Group O. Rh + ve	None		(1) Alive and well Rh + ve	1941	Live infant, $5\frac{1}{2}$ pounds. Group O, Rh + ve.	Repeated small haemorrhages from 28/52. Spontaneous delivery at 34/52. Placental insertion not determined by vaginal examination.
		(5) *Accidental Antepartum Haemorrhage—Mother and Father both Rh Negative.* (*Saint Alfege's Hospital*).					
5.	Group O. rh rh		rh rh	(Primigravida)		Infant lived only a few minutes. Cord blood unobtainable.	Scanty irregular haemorrhage from 28/52. Rupture of membranes at 36/52 for severe toxaemia. Placenta not felt.

Whether in such cases the risk to the baby from erythroblastosis is greater than the risk from prematurity; and that therefore induction rather than expectancy should be the line of treatment when possible, it is as yet impossible to say.

One fact is certain, the woman with antepartum haemorrhage is often likely to need a blood transfusion. Except in those units fortunate enough to be able to have all expectant mothers Rh-tested, or have a blood bank of only Rh negative blood, there is a grave risk of incompatible transfusion being given.

I have to thank Dr. Allott for his enthusiasm and untiring co-operation without which I could not have proceeded. My thanks are also due to the medical staff of Queen Charlotte's Hospital and to Dr. Young, Medical Superintendent and Miss Fleming, Obstetric Consultant, St. Alfege's Hospital, for permission to publish these cases.

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A Morphological Study on Chorioepithelial Proliferations
(Based on 10 cases).

BY

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THE basic principles of pathology are known to all but in the morphological study of human trophoblast—normal or pathological—difficulties arise in the proper interpretation of the findings. These are due to the complicated process of amalgamation of ovum with mother and the peculiar behaviour of the elements involved. So it is necessary to recapitulate the physiological changes in the early stages of normal placentation in order to appreciate the pathology of chorionic epithelium.

From a study of descriptions of placentation by Grosser,[1] Streeter,[2] Brewer and Fitzgerald,[3] Rock and Hertig,[4] and many others, explanation experiments *in vitro* by Friedheim,[5] Maximow,[6] and Sengupta,[7] as well as personal observations, an attempt will be made in this paper to elucidate more fully the relation of early trophoblastic development to either the normal or penetrating placenta, the simple or destructive hydatidiform mole, or, finally, the malignant variety of chorionepithelium—the chorionepithelioma.

PHYSIOLOGY OF THE TROPHOBLAST.

The modern conception of the trophoblast is that it produces the chorionic epithelium with all its cell types. Thus the polygonal cells or cells of Langhans and the syncytial cells must be considered to be successive stages of differentiation. In the earliest stages of development the trophoblast consists only of Langhans' cells which are able to propagate by cell division and to infiltrate and to destroy tissues like a malignant tumour. On the other hand the syncytium must be regarded as a secondary formation. This does not mean that it is purely a degenerative product. On the contrary, its cells display marked biological activity in their proteolytic ability to nourish the foetus in its early stages of development by liquefying the maternal tissues at a time when foetal villous vessels are not yet formed. The formation of syncytium apparently takes place whenever Langhans' cells come in contact with liquid material, or local conditions become less suitable for cell nutrition. This explains the appearance of syncytium in non-liquefied tissues. There are other kinds of chorionic cells which are important, especially when considering the pathology of the trophoblast. These have been described by different authors as "syncytial giant cells" or "migrating" or "chorionic single cells." Their origin from the cellular columns of the trophoblast has been definitely accepted as the result of Meyer's[8] studies on this subject. They may appear far from the placental site and can maintain themselves in the maternal tissues for a long period. Finally, mention must be made of the fibrinoid coagulation, product of degeneration of chorionic epithelium and maternal tissues. Grosser[1] first drew

attention to its homogeneous and more clumpy shape in contrast with the more fibrillar shape of blood fibrin. According to Meyer,[9] this fibrinoid coagulation must be considered a phenomenon of regression which is due to the struggle between foetal and maternal tissues and appears also as a demarcation zone between less vital tissues. Thus this fibrinoid coagulation is to be found always at contiguous surfaces in the so-called "stripe of Nitabuch." It can also be seen at the sites of irregular proliferation of the chorionic epithelium either in marginal vessels or in the depths of the myometrium. The stripe of Nitabuch may be considered as a kind of barrier against the invading trophoblast. It varies in thickness with the result that where it is particularly dense it will entirely check the progress of the invading trophoblast.

As soon as the trophoblast has developed its power to dissolve the maternal tissues the ovum imbeds itself wherever it may be situated at the time. At first these tissues become entirely liquefied but gradually the defence of the maternal body grows stronger, whereas the power of the blastic invasion weakens. Thus, the chorionic epithelium becomes intermingled with the maternal tissues and the ovum settles down within the maternal substance only by the action of the chorionic epithelium. All this occurs in the so-called "penetration zone" (Grosser) and this stage of trophoblastic development is described by Meyer[9] as the "histiotrophic" phase, which means that the trophoblast nourishes itself at the cost exclusively of the maternal tissues. This phase is marked by many changes leading gradually to the "haemotrophic" phase and the formation of the true placenta. The trophoblast has generally fulfilled its task within the first 8 or 10 weeks of pregnancy and later disappears, leaving behind only the epithelium of the villi. It is important to bear in mind that during the histiotrophic phase a foetal stroma does not exist generally, but where it does form, for example, in the first generation of villi, it has no biological function since it is not vascularized. Meyer[9] stresses this fact and calls this type of growth "cytotypic" as distinct from the "histiotypic" form of growth during the haemotrophic phase just mentioned. An appreciation of these different types of growth is essential, since it is only the first type, namely the "cytotypic," that is found in the chorionepithelioma, which thus occupies a unique position in human pathology.

It has been necessary to consider in full the features of the trophoblast's normal development since a knowledge of these is essential when one has to give an opinion on chorionic invasion, on abnormally active proliferation of chorionic epithelium, or whether a growth is benign or malignant. The basic elements which compose the final picture of all such cases are identical. They consist of:

(1) An unlimited power of destruction in the cells of the young trophoblast.
(2) The maternal defence-mechanism which comes into full action only slowly and progressively.

The occult potentialities and mutual balance of these factors are sometimes impossible to assess even by one who has had much experience in pathology.

Some of these difficulties in diagnosis regarding chorio-epithelial proliferations will now be described.

A. Chorionic Invasion.

Meyer[8] first emphasized the importance of the chorionic giant cells and their origin from the chorionic epithelium. In the literature of the distant past these cells have often been mentioned in connexion with so-called atypical cases of chorionepithe-

lioma. Meyer, and before him von Franqué,[10] doubted whether single chorionic cells were characteristic of a malignant tumour unless they appear in accumulations of cells—the third irregular type of chorionepithelioma (Marchand). Franqué was always surprised by the astonishingly high rate of complete recovery in cases of irregular chorionepithelioma with isolated cellular proliferation. Meyer[8] has clarified this problem by demonstrating that single chorionic cells in varying numbers were often to be found at the site of placentation, proliferating from the cell columns of the trophoblast into the decidua and even muscle layers. At the 4th or 5th month of pregnancy these cells are to be found in their greatest number and by the end of pregnancy they have become much fewer. On the other hand they may be observed in much larger numbers in the case of pregnancy in an abnormal uterus, where there is hypoplasia or atrophy of the mucosa, in endometriosis, or in an abnormal pregnancy such as hydatidiform mole or placenta praevia. Thus one can say a fully developed decidua acts as a sort of barrier against the abnormal proliferation of chorionic elements. Even if these cells are found in excessively large numbers, provided placental remains are present at the same time, there is no need for alarm. By the 4th week after delivery or abortion they have usually disappeared. But if these cells are found in rather considerable numbers after this time, without any other morphological changes due to pregnancy, then one must view the case with suspicion. In such a patient the pathologist should advise that a clinical examination and a quantitative estimation of the gonadotropic hormone in the urine be carried out every 2 or 3 weeks. If the findings are at first negative and later the test becomes positive, or if there is an increasing amount of gonadotropic hormone in the urine, then there is no doubt as to the existence of a chorionepithelioma or a destructive hydatidiform mole (Clauberg,[11] Ehrhardt and Bureck[12]). Four cases will now be described illustrating chorionic invasion. The cases were diagnosed as abortion 2, myoma 1, rupture of the uterus 1.

CASE 1. 837/40.

Patient aged 25. Amenorrhoea for 3 months. One week before admission to hospital had acute abdominal pain and some uterine bleeding. Diagnosis, abortion. Treatment, curettage.

Histology of curettings: blood, uterine muscular fibres and irregularly formed endometrium. Mucosa generally rich in glands of a multiform type. No active secretion. Stroma variable in its structure; sporadic formation of decidua compacta and small areas of dense inflammatory infiltration. In some places there are large irregularly-shaped strips of fibrin. Around the vessels there are big decidual cells mingled with much fibrin. In some parts the decidua reaches deeply into the muscular layer where large cells are rather frequently seen between the muscular fibres. Even with low power these cells, by reason of their irregular shape and darker colour, can be easily differentiated. They are found particularly near the vessels. They have one or several large round or ovoid nuclei and can be easily distinguished from the large decidual cells.

Diagnosis: Endometrium in a state of puerperal regression with inflammatory infiltration. Excessive proliferation of chorionic cells in the muscular layers of the uterus (chorionic invasion). No sign of malignancy in the material examined.

CASE 2. K.I. 3/39.

Patient aged 30; 5 years ago normal delivery; 2 abortions, 1 before and one after the delivery. No amenorrhoea but 2 short uterine haemorrhages a fortnight after the last normal period. Curettage. A small soft area was found on the posterior wall of the cervical canal.

Histology of the curettings: (Professor Oberndorfer, late Director of the Cancer Research Institute, Istanbul University.)

Puerperal stroma, vessels in regression, compressed gestational glands. Stroma extensively infiltrated by giant cells containing a few or many nuclei, as well as smaller giant cells resembling common decidual cells. Inflammatory infiltration (Fig. 1).

Diagnosis: ? Hyperplasia of decidua. ?Chorionic invasion. No sign of malignancy in the material examined, but further observation of the patient is recommended.

Case 3. G. 3/38.

Clinical data not available. Operation specimen of a uterus removed by subtotal hysterectomy.

Macroscopic findings: Myoma, size of a small apple, and, in addition, a round red area the size of a hazelnut, within the uterine muscle in the neighbourhood of one tube.

Histological findings: Muscle very vascular and containing detached endometrial glands. At one side of the section there is an area of compact round-cell-infiltration with some hyalin connective tissue. The patch of red necrosis observed macroscopically is adjacent to this area. The necrotic region consists of fibrin and blood and is everywhere surrounded by swollen fibrinoid coagulated muscle-fibres and strips of hyaline connective tissue. Big irregular cell-elements with large, compact and darkly stained or vacuolized nuclei are observed here very frequently. Within this region no signs of inflammatory infiltration (Fig. 2).

Diagnosis: Myoma of the uterus. Slight adenomyosis interna. Giant-cell-proliferation around a necrotic area (chorionic invasion).

Case 4. 817/38.

Patient aged 22; 3-para, 7th month of pregnancy.

Clinical diagnosis: Internal haemorrhage (?rupture of the uterus).

Treatment: Vaginal hysterectomy.

Macroscopic findings: A hole, diameter 2 cm., at the fundus uteri. Edges round and thick; at other places the uterine wall is particularly thin. Placental remains not seen.

Microscopic findings: Typical puerperal changes. At the placental site there is a more or less clearly visible stripe of Nitabuch separating the maternal from the foetal elements. Here there are large cellular accumulations, rather similar to the cell-columns of young trophoblast. At some other parts of the placental site separation of the maternal and foetal tissues is not so marked. At such places one finds an extensive invasion of large, irregularly shaped, one- or multi-nucleated cells, which can be seen deep in the muscular layer also. These cells form short lines and are surrounded by some inflammatory cells. The muscle-fibres next to the serous coat of the uterus are in some places replaced by connective tissue poor in nuclei.

Diagnosis: Spontaneous rupture of the uterus. Persistence of the trophoblast. Chorionic invasion.

Discussion.

In Case 1 there can be no doubt that the changes are benign. The histological picture is that seen after an ordinary abortion. Even though there is considerable chorionic infiltration it is not of much importance. However in Case 2 the cellular invasion is so striking that it seems easy to diagnose the condition as malignant. Professor Oberndorfer leaves the question open as to whether the case is one of excessive decidual reaction or chorionic invasion. I incline to the latter interpretation. Firstly, in cases with hypertension of decidua, giant-cell-formation is generally not so marked as in this case. Secondly, large parts of the stroma do not show decidual reaction at all, and infiltration is most widespread in regions where there are digitations of muscle-fibres into the mucosa. Thirdly, there is the clinical evidence of the soft area in the posterior wall of the cervical canal suggesting an unusually low nidation of the ovum. This would also support my view that this is a case of simple chorionic invasion. Case 3 is incomplete through lack of clinical data. The pathologist can describe only the presence of chorionic invasion following a supposed recent pregnancy. This diagnosis might be disputed on the insufficiency of clinical detail. However, one can exclude a giant-cell-reaction around a foreign body as well as

a regenerative reaction of muscle with formation of myogenic giant cells from the general histological picture. That the presence of a myoma and an endometriosis in this specimen would stimulate chorionic invasion is shown by de Snoo and Stroink.[13] In Case 4 the main findings are old scarring in the uterine wall, chorionic-cell-invasion and a partial persistence of the trophoblast. An exact evaluation of the aetiological relation of these facts is difficult. One is inclined to assume that the lesion of the uterine muscle may probably have induced the foetal parts to more intensive growth, which is further suggested by the presence of cell-columns in a rather late stage of pregnancy. There is, on the other hand, no morphological proof that the clinical catastrophe was mainly due to this fact. For the explanation of the rupture the presence of scars in the uterine wall seems quite sufficient. But, so far as the problems dealt with in this paper are concerned, it is interesting that the histological findings point to the existence of that intimate reciprocal interference of maternal with foetal parts mentioned in the introduction.

B. Chorionic Proliferation Together with Villous Stroma.

Examples will now be given of increased proliferative power of the chorionic epithelium. One case is a spontaneous rupture of the uterus, and the other two are hydatidiform moles.

Case 5. 847/39.

Patient, aged 25, admitted to hospital moribund. Uterus, size of a 7 months' pregnancy.

Diagnosis: Internal haemorrhage.

Autopsy: Three litres of fresh blood in the abdominal cavity. On the fundus of the uterus, which contained a normal pregnancy of 5 months, there was a bluish, round area 0.5 cm. in diameter through which chorionic villi were protruding. Examination after fixation revealed extreme general thinning of the uterine wall, a small rupture at the fundus and imminent rupture at 2 other places, where the uterine wall was about 1 mm. thick.

Microscopic findings: Destruction of uterine wall at the site of the rupture. Muscle shows extensive fibrinoid degeneration in some parts, and in others complete necrosis. Villi appear to be boring into the uterine wall, and chorionic elements, singly or in masses, are eroding and even completely obstructing the vessels (Figs. 3 and 4).

Diagnosis: Spontaneous rupture of the uterus "placenta percreta."

Case 6. 193/40.

Patient, aged 18, moribund. Uterus 6 months in size; excessive bleeding *per vaginam*.

Autopsy: Uterus 22 by 14 by 10 cm. with cystic ovaries. Peritoneal surface regular. Cavity contained hydatidiform mole of medium size, grape-like clusters with much blood and clot. Uterine wall of regular thickness of about 1 cm. Only at the placental site was the wall somewhat thinner. Vessels engorged with blood. Apart from the presence of a mole and absence of a foetus the uterine topography was that of a normal pregnancy. Decidua vera with an average thickness of 2 mm. was clearly seen and lifted from the underlying tissues. The serotina is generally well formed but variable in thickness. Fallopian tubes twisted, abdominal ostium open. Each ovary about the size of a hen's egg and consisting of several small cysts with a yellow surround.

Microscopic findings: Uterine wall at site of molar attachment (from within out, Fig. 5), molar tissue consisting of large villi with rather dense or dropsical stroma and double layered epithelium; decidua compacta contains much fibrin; decidua spongiosa in this situation does not show important pathological changes, but clear demarcation from the muscular layer which has enlarged veins filled with erythrocytes and inflammatory cells. But in other places the spongiosa and layer of fibrin are greatly reduced in their thickness and there is no line of distinction between them. In general the chorionic elements have not passed through the fibrin into the deeper layer of the decidua, but there are places where they reach the muscular layer in large numbers followed closely by villi. In nearby areas both layers of the mucosa

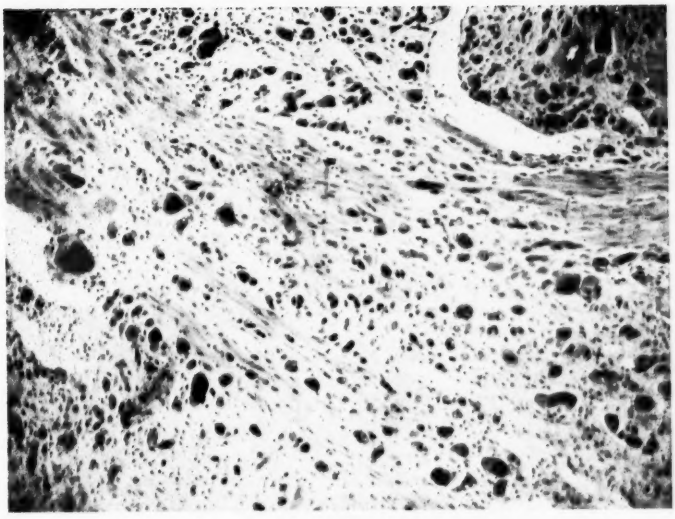

FIG. 1 (CASE 2).

Endometrium showing infiltration by many mono- and multinuclear giant cells. ×60

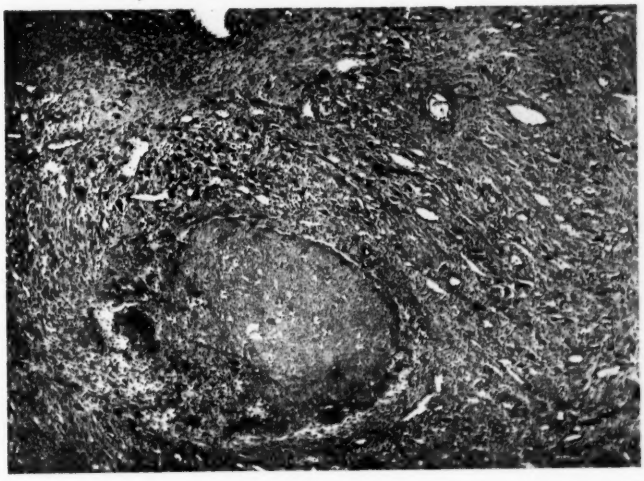

FIG. 2 (CASE 3).

Uterine wall showing giant cell infiltration around necrotic area. ×21.

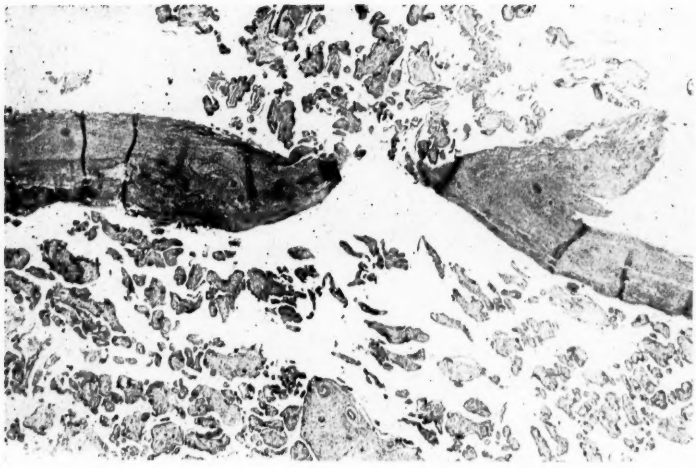

FIG. 3 (CASE 5).

Uterine wall at site of rupture.
×6.

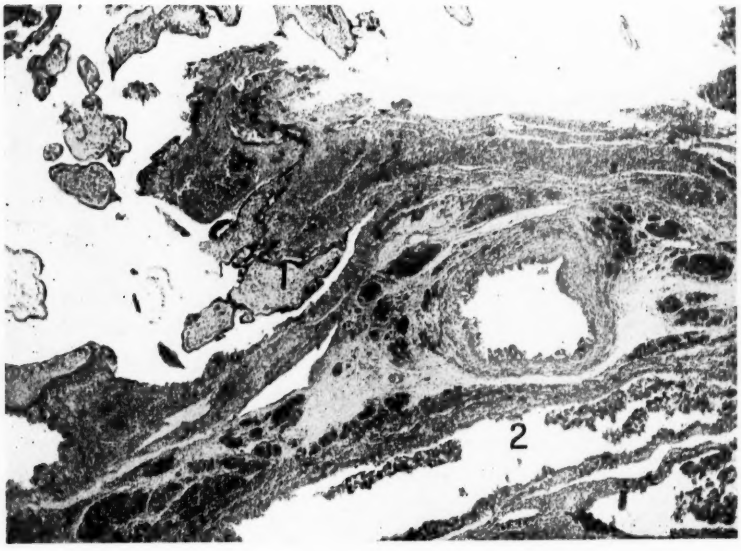

FIG. 4 (CASE 5).

Uterine wall showing at (1) attachment of chorionic villus directly to muscle, at (2) enlarged vessels containing many chorionic cells. ×21

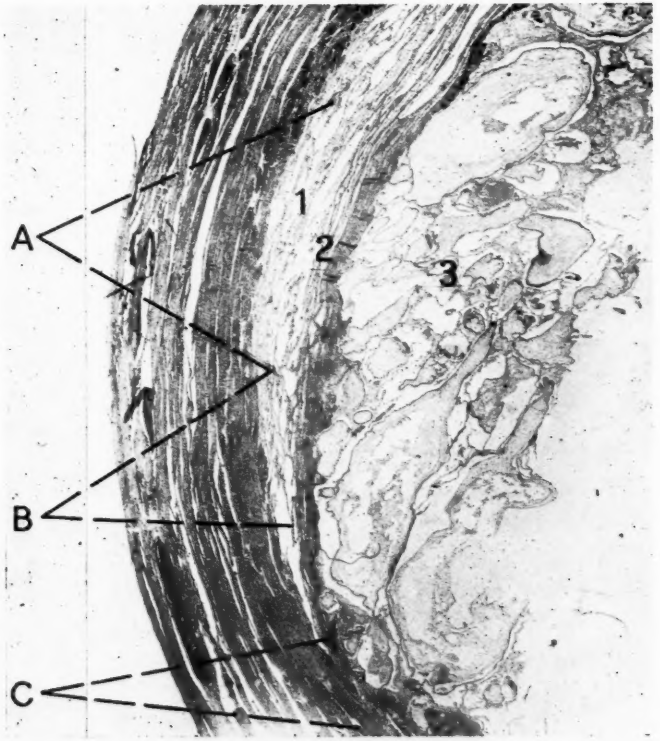

FIG 5 (CASE 6).

Hydatidiform mole *in situ*. Placental site.

A. Shows region of fully-developed mucosa (1) and wide fibrin layer (2) between mole (3) and mucosa.

B. Shows thinning of mucosa.

C. Shows direct contact of mole with muscle. ×6

W.A.L.

FIG. 6 (CASE 7).

Composite photomicrograph of transverse section of uterine wall.

A Peritoneal surface. B Cavity.

Typical of destructive hydatidiform mole. ×4

FIG. 7 (CASE 7).

Vaginal metastasis showing large well-formed placental villus (1) and placental villi without epithelium (2). ×21

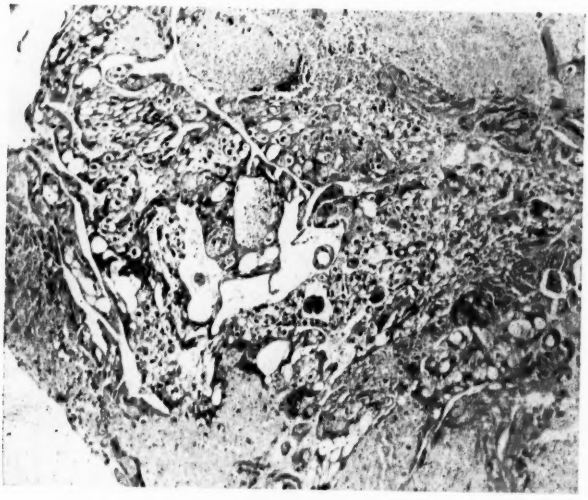

FIG. 8 (CASE 10).

Curetting showing the only area where chorionic elements were present and on which the wrong diagnosis of chorion-epithelioma was based. ×21

seem to have disappeared owing to the massive infiltration of chorionic cells disregarding any pre-existent layers and undermining the margin of the neighbouring tissues. Here even the superficial venous sinuses are open and are invaded by chorionic cells which, however, are still attached to villi. The penetrating elements consist mainly of small Langhans' cells with very few syncytial cells. Few degenerative changes are to be seen in these cells and haemorrhagic areas are rare.

Uterine wall opposite to molar attachment: Normal decidua compacta with a wide spongiosa is sharply delimited from the muscle layer. Vessels open and enlarged.

Specimens from the centre of the mole: These show different degrees of epithelial proliferation. Syncytial elements observed more frequently. The average extent of the epithelial proliferation is not excessive.

Diagnosis: Hydatidiform mole *in situ*.

CASE 7. 506/41.

Patient, aged 22. Admitted to the hospital in a very anaemic state. Examination revealed hydatidiform mole, which was removed *per vaginam*. Two months later the patient returned because of uterine bleeding and a small nodule at the introitus. While in hospital there was severe haemorrhage from this.

Clinical diagnosis: Chorionepithelioma following hydatidiform mole. Treatment was hysterectomy and removal of the vaginal nodule.

Pathological examination.

(1) Hydatidiform mole. This consisted of large masses of vesicular tissue and weighed 1800 g. Histologically, thick large villi with extremely dropsical stroma. Epithelium in certain parts shows excessive proliferation with preponderance of syncytial elements. Where Langhan's cells are seen in great numbers they are surrounded by much fibrin. On some of the villi there are large cushions of well-preserved Langhans' cells. Here and there are necrotic areas.

Diagnosis: Hydatidiform mole with extremely marked epithelial proliferation.

(2) Operation specimen; macroscopic findings: Uterus (7 by 6 by 4 cm.) with adnexae. Surface regular, consistence solid, colour pale yellowish. The surface of the mucosa is very irregular. There is an elevation, the size of a cherry stone, near the internal os, in which could be seen small vesicles. There is a similar finding at the uterine end of the left Fallopian tube. On the uterus opposite to the first-mentioned elevation there is a small, round, reddish nodule lying partly within the myometrium. The colour of the mucosa varies from greyish yellow to red. The demarcation between the endometrium and myometrium is generally well defined. The myometrium is solid and the vessels clearly distinguished. Sections made through the myometrium in many different planes a few mm. from each other show that there are yellow lines running from the mucosa into the depth of the muscular layer, where they open out into what resembles small honeycombs (Fig. 6). In places these are the size of a cherry and villi can be seen within even by the naked eye. Such formations are to be seen throughout the whole length of the uterus. The Fallopian tubes twisted and a little thickened. Ovaries each the size of a walnut. They contain small cysts which are surrounded by wide yellow borders. The nodule in the vagina measures 2 by 2.5 cm. and is friable.

Microscopic findings: The endometrium in some places appears fairly normal. It is poor in glands but shows some inflammatory infiltration. In other places there are typical puerperal changes such as extensive chorionic invasion, thickening and hyalinization of vessel walls, much inflammation and a little necrosis. However, in many other parts chorionic tissue—villi and epithelium always closely connected—proliferates into the muscular layer. But these proliferations are generally separated from the muscle proper by a wide layer of dense fibrin. Here and there foetal cells are to be seen lying in the vessels. These changes can also be seen in the deeper layers of the endometrium where larger masses of Langhans' cells and syncytial elements are generally found together with the villi or at least having taken their origin from a villus. Haemorrhagic areas are completely absent. The inflammation is less in the deeper layers of the muscle. At each cornu of the uterus very active chorioepithelial proliferation can be seen but without any reaction of the surrounding tissues.

Fallopian tubes: No pathological changes.

Ovaries: Many small cysts in the ovarian stroma containing masses of large luteal cells. Atretic

follicles show wide borders of theca interna cells. In one place there is a ripening follicle with a zone of granulosal cells, but only a few primordial follicles.

Nodule from vagina: Sections consist of old blood, abundant fibrin, lymphocytes and polynuclear leucocytes.*

Mingled with these elements villous stroma without epithelium is frequently seen but in some places villi are seen with well-preserved epithelium. Rarely, degenerating chorionic cell elements are found (Fig. 7).

Diagnosis: Destructive hydatidiform mole with excessive epithelial proliferation and a metastasis in the vagina. The findings do not support the existence of a chorionepithelioma.

Discussion.

It is extremely rare that a placenta with normally shaped villi has such destructive power as that seen in Case 5. Space forbids discussion of this phenomenon and whether it was due to an increased proliferative tendency of the chorionic cells or to a breakdown of the maternal defensive power. This case is described in order to show that enormous destruction may be found even where there is a morphologically unaltered chorionic epithelium. It is common to find a hydatidiform mole that penetrates deeply but it is the extent of the proliferation that varies. Case 6 is a rare one, for it shows a hydatidiform mole *in situ* penetrating deeply into the muscle. So also with Case 7, where an excessive proliferation of the chorionic epithelium and a metastasis in the vagina were found. This combination made diagnosis difficult. To this problem we shall refer later when discussing the subject of malignancy in chorioepithelial proliferations.

* Ladewig's[14] modification of Mallory's stain is a great help since it facilitates the differentiation of tissues even in necrobiosis. This is especially useful when examining material with puerperal changes.

The following facts need to be borne in mind when considering penetration by chorionic elements. The serotina is invaded by chorionic cells. These completely infiltrate the maternal tissues which become compressed and may perish from pressure atrophy. The villi—normally shaped or degenerate—together with the chorionic cells may now penetrate to such a depth that they reach the superficial or even deeper veins of the uterine wall. It is obvious that whole villi or isolated chorionic epithelial cells having reached these veins may find their way into other vessels without difficulty. Their ultimate destination depends on whether or not these cells can still multiply. Epithelial cells of the normal placenta have not this ability. But occasionally they may grow further ahead within the vessels, destroy neighbouring tissues and even break through into other vessels. In this way they cause extremely heavy destruction. Even so this penetration, according to general pathological principles, must still be regarded as a benign one owing to its continuity of growth and its histiotypic form (epithelium and stroma being always together).

Penetration is an attribute of the normal trophoblast and so, in the examination of pathological changes in the chorionic epithelium, one must not attach too much importance to this finding alone. Fig. 4 (Case 6) shows very clearly the thinning of the serotina at one place and villi coming gradually into the most intimate contact with muscle where penetration reaches its maximum. The real destruction in these regions is not as great as would be expected, because the spaces filled with villi and epithelial cells are not the results of a process of liquefaction of the tissues but, in fact, are simply wide veins of the placental site. In some places the walls of the vessels can still be clearly defined. In Case 7 penetration is wider and deeper and is not limited

to the region of the placental insertion. Small fragments of the mole appear close to the peritoneal surface of the uterus and even to the interstitial portions of the Fallopian tubes. That the epithelium of the villi still possesses remarkable proliferative power is proved by the observation that the largest accumulations of chorionic fragments are to be seen at some distance from the cavity of the uterus. As a structural element the epithelium in Case 7 does not play such an important *rôle* as in Case 6. But chorioepithelial cells may be endowed with considerable destructive power even though there may not be any visible signs of activity (see Case 5, "placenta percreta"). Thus proliferation of chorionic epithelium brings up the recurring question as to when and in what circumstances such proliferation should be regarded as the expression of malignant or benign growth. Most authors who have studied this problem agree that there are some cases in which the above distinction cannot be made by morphological methods alone, although sometimes a careful review and follow-up of a case may eventually lead to its proper interpretation.

Two of the essential characteristics of malignancy—invasion and destruction—are not usually applicable when dealing with the elements of chorionic epithelium. We have already mentioned the similarity between the young trophoblast and chorionepithelioma and have stressed the fact that the main attribute of the chorionepithelioma is its reversion to cytotypic growth. As long as epithelium is found in connexion with villous stroma the morphological proof of its being an independent and cytotypic growth will be extremely difficult, although the possibility of a change from a simple or destructive mole into a chorionepithelioma can never be excluded. However, for diagnosis of malignancy one would insist that the bulk of epithelial cells should clearly predominate over the stromal, and further, that independent epithelial proliferation should be seen in at least one place. In Case 7 (destructive mole) the tissue as a whole shows signs of exceptionally vigorous proliferation which is less where it has penetrated most deeply. Considerable epithelial proliferation independent of villous stroma was not seen either in the mucosa or in the muscle of the uterus. The way in which the chorioepithelial cells, mostly Langhans' cells, come into contact with muscle resembles closely what is seen in the young trophoblast of extrauterine pregnancy. Meyer[9] has drawn particular attention to this. In Case 6 (hydatidiform mole *in situ*) there is considerably more epithelial proliferation, and its interpretation depends on the topographical relations of the elements concerned. The anchoring villi of the mole show marked penetrative power. In normal pregnancy villi are commonly found, adjacent to maternal tissue, showing quite thick club-like swellings due to increased proliferation of their cells. It is only to be expected, therefore, that features similar but more striking would be found in cases of hydatidiform mole. These are due to the generally enhanced capacity for growth of the chorionepithelium in this condition. Thus, in this case, there is no doubt that in spite of the strong tendency to proliferation, destruction and infiltration, the only diagnosis that could be considered was that of a benign mole. The features were simply those, but in excess, of the physiological process of nidation.

In Case 7, the significance of the vaginal metastasis remains to be explained. Schmorl[15] was the first to demonstrate that transportation by the bloodstream of whole villi or isolated chorionic cells is almost a feature of normal pregnancy. He has found such cells within the smaller arteries and capillaries of the lungs. In normal preg-

nancy they disappear in a short time. Furthermore in cases of early abortion or hydatidiform mole he has occasionally observed proliferations of displaced chorionic cells growing through the walls of vessels and even infiltrating neighbouring tissues. He explains this phenomenon as due to cell casts of somewhat pathologically altered chorionic epithelium. The elements concerned may go on proliferating for a limited period but will finally be mastered and eliminated by the maternal defence-mechanism. These findings raise the question, in cases of hydatidiform mole with displacement of chorionic cells and their proliferation in other parts of the body, as to whether or not these should be regarded on principle as an expression of malignant growth. There are, of course, numbers of cases cited in which a hydatidiform mole has been followed by metastases showing histologically every sign of a chorionepithelioma. Such a case has been reported by Brews[16] and a similar one will be described later in this paper. On the other hand there are cases where the histology is not so definite. Gygax[17] published a case in which a typical metastasis of a hydatidiform mole was removed from the vulva. There was not any sign of malignant growth in the uterus, and at autopsy (the patient died of an intercurrent illness) all internal organs were free from metastases. Wegelin,[18] too, has demonstrated the benignancy of a metastasis in the vulva, free even of villi, in a case of hydatidiform mole. In this case the histological picture, with regard to the occurrence of isolated cells, fibrin and fibrinoid degeneration, resembles that found during normal placentation in the uterus. The chorionic cells seem actually to be submerged by the masses of fibrin and, as numerous degenerative forms of cell nuclei were to be found, Wegelin concluded that the vulval metastasis in this case must be considered as one of degeneration which would probably have disappeared without surgical removal. These observations show that the presence of metastases is proof of malignancy only in so far as tumours arising from the individual's own cells are concerned, but in the case of proliferation of foetal cells the above dictum does not necessarily apply. In Case 7, well-preserved and degenerate villi were found but no coherent epithelial cell masses, so one is of the opinion that even the presence of the metastasis does not alter in any way our opinion as to the benignity of the process concerned.

C. Chorionic Proliferation Without Villous Stroma.

Three cases will now be described. The 1st is a typical chorionepithelioma with a metastasis in the vagina, the 2nd is a post-partum chorionepithelioma and the 3rd will be discussed separately as there was an error in diagnosis.

Case 8. 611/40.

A married woman, aged 17, became pregnant a month after marriage and complained of a brown discharge. At the 4th month there was a haemorrhage and she passed some meat-like tissue. During the following 4 months she was curetted 3 times by 3 different doctors. The first curettings were reported to be those of a hydatidiform mole. On arrival at hospital she was suffering from anaemia and on pelvic examination a red swelling the size of a hazelnut was found on the anterior vaginal wall. The rest of the organs were normal. A biopsy of the swelling showed it to be a chorionepithelioma. Hysterectomy was performed. On discharge from hospital 7 weeks later no vaginal nodule was to be found. Seven months later the patient wrote that she was quite well.

Macroscopic findings:

(1) Nodule from vagina, soft, haemorrhagic and friable.

(2) Uterus with adnexae. In the anterior uterine wall 3 reddish nodules the size of a pea could be enucleated easily. Uterine mucosa thickened but

regular. At the level of the internal os there was another small nodule. The left ovary was cystic. In the left mesovarium there was a dark red, soft nodule of the size of a cherry stone.

Microscopic findings: All the nodules show haemorrhagic necrosis. In several places, especially in the vaginal nodule, numbers of well-preserved Langhans' cells, rare syncytial elements and no villous stroma are to be seen.

Diagnosis: Typical chorionepithelioma with a true metastasis in the vagina.

CASE 9. 247/42.

Married woman, aged 30; 6 full time deliveries and 2 abortions. Patient came to hospital a week after the last delivery complaining of bleeding. Pelvis normal for the period of puerperium. Bleeding ceased and patient discharged; returned to hospital 3 weeks later with severe haemorrhage, very anaemic. The uterus was larger than at examination 4 weeks previously. Curettage was immediately performed. Histological diagnosis, chorionepithelioma. Her condition contra-indicated operation. Twelve days later X-rays showed a normal lung picture. A second X-ray was taken a fortnight later, and showed a shadow the size of a small fist, in the lower lobe of the right lung. She died 14 weeks after delivery. A few days before death there was in the urine a content of 175,000 mouse units per litre of gonadotropic hormone.

Autopsy showed chorionepithelioma of the uterus; multiple metastases of parametrium and both lungs; purulent thrombophlebitis of all pelvic veins up to the vena cava.

Microscopical findings: In many areas of the uterine mucosa there were irregular masses of Langhans' cells and syncytial elements in great number, and these extended into the myometrium causing much destruction of uterine tissue. In the vessels were found elements of the tumour as well as the typical changes of purulent thrombophlebitis. In the lung metastases the tumour was well preserved, there being little necrosis.

DISCUSSION

The vaginal biopsy of Case 8 showed, besides blood and fibrin, large groups of Langhans' cells. The diagnosis of chorionepithelioma was obvious. This was confirmed by the case history which showed a clear relation between the hydatidiform mole and the vaginal metastasis. The size of the uterine tumour was unusually small but at the same time it was obviously a typical chorionepithelioma. The repeated curettages may have interfered in some way with the proliferation of the tumour and also the small hormone content of the urine (25,000 mouse units per litre) may be similarly explained. In Case 9 the history was one of postpartum haemorrhage and one would have expected the curettings to have revealed fragments of the placenta or else puerperal endometritis. One would not have expected chorionic epithelium. However, as masses of chorionic epithelial cells, Langhans' and syncytial cells were seen, the diagnosis of chorionepithelioma became obligatory. The subsequent course of the case put the diagnosis beyond all doubt.

CASE 10. 647/41.

Married woman, aged 29; 3 children; 1 year ago induced abortion (4th month). Menstruation usually regular. Last period a fortnight before admission to the hospital. A brisk haemorrhage the night before admission. Haemoglobin 50 per cent (Sahli).

Pelvic examination: Uterus a little larger than normal, external os 1 finger dilated. Curettage performed.

Microscopic findings: Endometrium in secretory phase. Areas of fibrinoid coagulation, and, in contact with these, a tissue consisting of 2 types of cells.

(1) Rather large cells with central nucleus and clear protoplasm arranged in groups (Langhans' cells).

(2) Large confluent elements with varying shapes of nuclei, darkly stained, protoplasm often vacuolated (syncytial elements).

No villous stroma. The syncytial formations are more numerous than Langhans' cells. Three days after curettage the Aschheim-Zondek test with undiluted urine was positive, but was negative in

dilution corresponding to 25,000 mouse units per litre.

A tentative diagnosis of chorionepithelioma was made and the gynaecologist informed that the case should be carefully observed. The gynaecologist decided to perform immediate hysterectomy. A careful histological examination of the specimen showed a perfectly normal uterus. There was no sign of recent pregnancy.

Discussion.

In view of the fact that the uterus did not show the existence of a chorionepithelioma one needs to reconsider the diagnosis which was based on the histological picture of the curettings. Was it possible that the whole of the tumour had been removed by the curettage and that we had been fortunate enough to have seen this? This explanation must be dismissed, since the penetrative power of chorionepithelioma is so great and in the specimen we did not see any penetration into the wall of the uterus. On further reflection it is now obvious that the tissue which we saw in the curettings was not a chorionepithelioma but a simple trophoblast. We were misled because of its highly pleomorphic cellular composition as well as by the complete lack of villi and other puerperal characteristics. We did feel that our diagnosis had to be made with some reserve and at the time informed the gynaecologist of our doubt. However, he was guided by Hirschmann's old dictum that in a doubtful case it is wiser to sacrifice the uterus than to risk the life of the patient.

Conclusion.

(1) Isolated chorionic cells *per se* are but an indication of a state of pregnancy either present or past. When large numbers of invading cells are found this usually points to some previous abnormality of the uterus, such as myoma, adenomyosis, or old lesions —particularly when found a long time after pregnancy—and not to increased, independent activity of trophoblastic derivatives. It always remains with the pathologist, by all the means at his disposal, to establish a relation between chorionic invasion and pregnancy.

(2) The wide range, variations and distribution of cell proliferation and infiltration have been abundantly demonstrated in the above cases. One has purposely selected border-line material in order to emphasize the complexity of the problem and to show the difficulty in reaching a decision as to whether the condition is one of malignant chorionepithelioma or vigorously growing young trophoblast or hydatidiform mole. In these cases the pathologist must of necessity rely on the clinical findings, and especially the history and hormone estimations.

(3) One has attempted to explain that the presence of chorionic cell proliferations in the last month of pregnancy, after a full time delivery, or after an expulsion or removal of a hydatidiform mole supports the diagnosis of malignant chorionepithelioma. When similar histological pictures are present in a still existing mole or early pregnancy then one needs to be most cautious in making the diagnosis of malignancy.

(4) In the same way vaginal metastases are not necessarily malignant. When villous stroma is found in these then one is of the opinion that the condition is innocent.

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The Effect of Postoperative Exercises and Massage on the Incidence of Pulmonary Embolism at Chelsea Hospital for Women

BY

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FOR many years the high incidence of pulmonary embolism caused anxiety among the members of the medical staff at Chelsea Hospital for Women. This increased considerably when, in 1936, 50 per cent of the deaths following operations were due to pulmonary emboli.

It was therefore decided at the beginning of 1937 to establish a massage department which was placed under the supervision of one of us (I.C.S.). The duties of the members of the massage team were to instruct and supervise postoperative exercises, and to carry out massage in all cases after abdominal operations and operations for the repair of genital prolapse. The routine following minor operations remained unaltered, and special exercises and massage were not given after such procedures as curettage, insertion of radium, insufflation, etc.

Originally it was intended that the problem be reviewed after 3 years and the incidence of embolism compared in the years preceding and following the introduction of the massage department. Unfortunately the war intervened and detailed study of results was not made. However the experiment was considered a success, as not only did the number of cases of embolism decrease, but the general condition of the patients on discharge from hospital was obviously greatly improved.

The purpose of this paper is to study the effect of postoperative exercises and massage on the incidence of fatal pulmonary embolism. Non-fatal embolism has not been included as it was found that satisfactory details were not always available in the case notes.

A 14-year period is reviewed and is divided into 2 sections. The first, 1930 to 1936, consists of the 7 years before, and the second, 1937 to 1943, the 7 years after the institution of the massage department.

It is also intended to consider the deaths from embolism collectively and to study such factors as age, type of operation, etc. In addition some details of the type of exercises and massage now being employed at the hospital will be given.

INCIDENCE OF FATAL PULMONARY EMBOLISM FOLLOWING ABDOMINAL OPERATIONS.

A. 1930–1936. In this period there were 4,596 abdominal operations followed by 19 deaths from pulmonary embolism, i.e., the mortality from pulmonary embolism was 0.415 per cent or 1 fatal embolism followed every 240.5 abdominal opera-

tions. None of these deaths took place during operation.

B. 1937–1943. In this period there were 3,436 abdominal operations with 9 deaths from pulmonary embolism. In 3 of the 7 years there were no deaths from this cause.

Of the 9 deaths 2 may be excluded for the following reasons. The first, in 1938, took place on the 6th day after operation, but owing to a temporary shortage of staff the patient received no postoperative exercises or massage. The second, in 1943, is excluded as the embolism occurred during the operation.

Excluding these 2 cases the mortality from pulmonary embolism after abdominal operations from 1937 to 1943 was 0.203 per cent, or 1 death followed every 490.5 operations.

The incidence of fatal embolism after abdominal operations was therefore reduced by more than half following the introduction of postoperative exercises and massage.

Incidence of Fatal Pulmonary Embolism Following Operations for the Repair of Genital Prolapse.

In each of the 7-year periods there were 2 deaths from pulmonary embolism following roughly equal numbers of operations for prolapse.

Although postoperative exercises and massage have not reduced the number of fatal emboli following these operations, we have been impressed by the marked improvement in muscle tone and posture in this group of patients.

In 1938 Fletcher Shaw and Rickards[1] investigated the incidence of fatal pulmonary embolism after gynaecological operations during a 12-year period at Manchester Royal Infirmary, where exercises are carried out as a routine, and at St. Mary's Hospital, where exercises are not included in the postoperative treatment. Fatal embolism was found to be 5 times more common in the latter hospital. The authors do not differentiate between abdominal and other operations, and details of the exercises employed are not given.

General Review.

During the 14-year period 1930 to 1943 there were 21,066 operations at Chelsea Hospital for Women followed by 202 deaths. Of these 202 deaths 40, or 19.8 per cent, resulted from pulmonary embolism, i.e. the incidence of fatal embolism was 0.19 per cent, or 1 such death occurred in every 526 operations. Matas[2] found that the general prevalence of fatal pulmonary embolism in Europe and America in 2,196,834 operations from 1913 to 1931 was 0.27 per cent or 1 death from embolism in approximately every 500 operations.

According to Henderson[3] at the Mayo Clinic during the 10-year period ending in 1927, 6 per cent of all deaths following operation were due to pulmonary embolism. In our series 19.8 per cent of the deaths were due to pulmonary embolism, a much higher figure. This may be due to the fact that a high proportion of the operations (38 per cent) were abdominal.

Of the 40 deaths due to embolism 28, or 70 per cent, followed abdominal operations. Figures from similar series quoted in the recent literature are as follows: Graves,[4] 65.3 per cent; Henderson,[3] 80.7 per cent, Patey,[5] 86 per cent; Petren,[6] 88 per cent.

Age Incidence.

The 40 cases of fatal embolism can be grouped with regard to age as in Table I.

Table I.

Age group	Deaths from embolism
20 to 29 years	2 or 5 per cent
30 to 39 ,,	4 or 10 ,,
40 to 49 ,,	11 or 27.5 ,,
50 to 59 ,,	15 or 37.5 ,,
60 to 69 ,,	8 or 20 ,,

Five hundred consecutive cases admitted to hospital for operation in 1943 were grouped in a similar way according to age, (Table II).

TABLE II.

Age group	Percentage
20 to 29 years	24.4
30 to 39 ,,	37
40 to 49 ,,	22.6
50 to 59 ,,	10.2
60 to 69 ,,	4

With the aid of Table II correction was made and an approximate idea of the true incidence according to age was obtained.

From Table III it can be seen that post-operative fatal embolism becomes progressively more common in the higher age groups with a maximal incidence between 60 and 69 years. The average age of the patients was 50.5 years. In Henderson's[3] series of 313 fatal cases of embolism the average age was 53.2 years and Graves'[4] found that in a series of 194 cases the most common age of occurrence was in the decade 61 to 70 years.

TABLE III.

Age group	Corrected incidence
20 to 29 years	1.9 per cent
30 to 39 ,,	2.6 ,,
40 to 49 ,,	11.7 ,,
50 to 59 ,,	35.4 ,,
60 to 69 ,,	48.2 ,,

NATURE OF OPERATION.

A. Abdominal operations.

In Table V the abdominal hysterectomies for the two 7-year periods are listed. It is of interest to note the increase in the proportion of total hysterectomies in the 2nd period and the decrease in numbers of the Wertheim operation.

TABLE IV.

Operation	Number of cases of fatal embolism 1930–36	1937–43	Total
Subtotal hysterectomy with or without removal of appendages	5*	5	10
Total hysterectomy with or without removal of appendages ...	6	1†	7
Wertheim's hysterectomy	3	0	3
Laparotomy for malignant disease	2	1	3
Ventral suspension	1	0	1
Laparotomy for innocent conditions	0	1	1
Myomectomy and ovarian cystectomy	1	0	1
Ovariotomy and ventral fixation	1	0	1
Repair of ventral hernia	0	1	1

* In one case perineorrhaphy was also performed.
†Embolism occurred during the operation.

TABLE V.

Operation	1930–36	1937–43	Total
Subtotal hysterectomy with or without removal of appendages	1338	930	2268
Total hysterectomy with or without removal of appendages ...	793	948	1742
Wertheim's hysterectomy	144	61	205

Incidence of death from pulmonary embolism after:

Subtotal hysterectomy with or without removal of appendages, 0.449 per cent.

Total hysterectomy with or without removal of appendages, 0.401 per cent.

Wertheim's hysterectomy, 1.46 per cent.

There is no marked difference in the incidence of fatal embolism following the subtotal and total operations, but as might be expected it is much higher after Wertheim's hysterectomy.

B. Non-abdominal operations.

In the 14-year period there were 12 deaths from embolism following 13,061 non-abdominal operations or 1 death occurred in every 1,088 operations. It is of interest to note that 4 of the deaths followed the insertion of radium, 3 for malignant disease and 1 for an innocent condition.

Nature of Disease.

Of the 40 fatal emboli 13 followed operation for malignant disease, 10 abdominal and 3 non-abdominal operations.

Time of Occurrence of Pulmonary Embolism.

Of the 39 emboli which occurred in the postoperative period 17 occurred in the 1st week (all between the 3rd and 7th days), 11 in the 2nd week, 11 in the 3rd, and 1 in the 4th week. The nature of the operation, abdominal or non-abdominal, did not affect materially the time of onset of the embolism. Thus following abdominal operations there were 10 deaths in the 1st week, 7 in the 2nd, 9 in the 3rd, and 1 in the 4th week.

Presence of Pyrexia Preceding Embolism.

In a series of 146 fatal cases Robertson[7] found unexplained moderate fever in 18 per cent during the postoperative period. In our series of 40, only 32 temperature charts were still available. In 25 of these, or 78.1 per cent, some elevation of temperature was present during the 3 days immediately preceding the fatal embolism. This generally took the form of a mild intermittent pyrexia ranging from 99 to 100.5°F.

Brief Outline of the Exercises and Massage Employed.

The main aims of treatment are as follows:

1. Increased respiratory excursion resulting in improved venous return to the heart.
2. Improvement of the circulation and maintenance of muscle tone in the limbs.
3. Strengthening of the abdominal and perineal muscles and later the development of correct posture.

Abdominal operations.

The patient receives instruction in breathing exercises on the day before operation. These are commenced on the day following operation and she is encouraged to carry out active foot exercises, namely bending, stretching and rolling of the foot. On the 3rd day quadriceps contractions, gluteal contractions and more extensive foot movements are added and gentle massage of the legs is begun.

After the abdominal clips have been removed abdominal and gluteal contractions are introduced, and adduction exercises to improve the tone of the muscles of the pelvic floor.

Later the exercises are carried out with the patient's legs over the side of the bed, and trunk rotation, flexion and extension are begun. Eventually the standing position is adopted during the exercises and care is taken that the correct posture is being achieved. The patient leaves hospital with instructions to continue the exercises at home for at least a further 2 weeks.

Operations for the Repair of Prolapse.

A similar routine is employed, but perineal exercises are not introduced until after the 10th day to avoid unnecessary discomfort from stitches.

Discussion.

Much useful work has been carried out in recent years in an attempt to discover the aetiology of postoperative thrombosis and embolism. Perhaps the most productive has been the investigation of the constituents of the blood, particularly those taking part in the process of coagulation. Among others Atkins[8] has shown that there is a fall in the platelet count after operation followed by a sharp rise beginning on the 7th day and reaching a maximum about the 10th day. Robertson[7] found that the coagulation time was shortened and the sedimentation-rate increased. As these changes take place after every operation it is unlikely that they are the only factors leading to embolism.

Infection may play a part, and we have shown that in 78 per cent of our fatal cases some elevation of temperature was present during the 3 days preceding the embolism. As both Robertson[7] and Bonney[9] have pointed out, frank thrombophlebitis rarely precedes pulmonary embolism since the clot then is so adherent to the inflamed vessel wall that it cannot readily break loose. The infection is therefore probably of a mild type, insufficient in itself to produce an obvious phlebitis, yet of some importance in the production of thrombosis and embolism.

Most authorities are agreed that one of the principal contributory factor is venous stasis. This results from the relatively immobile position of the patient in bed, from obstruction such as that produced by the knee pillow and from diminished respiratory excursion. The venous return to the heart is dependent largely on the negative pressure in the thorax during inspiration and, at the same time, on the increased abdominal pressure resulting from descent of the diaphragm. In the limbs contraction of the muscles encourages movement of the blood in the veins.

In the past various types of prophylactic treatment have been suggested, many directed against the changes in the constituents of the blood. Thyroid extract, a diet low in fat and proteins, and anticoagulants such as heparin have been used with varying success. The most profitable lines of treatment however have been those directed to combating venous stasis. The simple expedient of raising the foot of the bed several times daily may be of some value, but we are of the opinion that stasis can best be prevented by active exercises and massage. Breathing exercises, abdominal massage and pressure applied particularly during inspiration, and active movements of the limbs encourage venous return to the heart. These should be commenced as soon as possible after operation, as in our series 43.5 per cent of the cases of fatal embolism occurred in the 1st week.

At Chelsea Hospital those who have undergone abdominal operations or operations for the repair of prolapse are the only patients who receive the benefits of postoperative exercises and massage. We believe that these could be extended advantageously to selected cases after minor procedures. We agree with Snell[10] who says "It is probable that there is a group of patients over 50 years of age, obese and with a normal or subnormal blood-pressure, who are particularly susceptible to pulmonary embolism as a postoperative complication," and we would add that this is even more likely in the presence of malignant pelvic disease.

SUMMARY.

Postoperative exercises and massage were introduced at Chelsea Hospital for Women in 1937 in an attempt to reduce the incidence of pulmonary embolism.

The incidence of fatal embolism following abdominal operations fell by more than 50 per cent in the subsequent 7-year period.

The deaths from embolism are reviewed with regard to general incidence, age of patient, type of operation, etc.

Some details of the exercises and massage employed are given and are followed by a short discussion with references to recent literature.

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A Short Study of Histaminase Activity During Pregnancy

BY

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INTRODUCTION.

Histaminase, first described by Best and McHenry[1] is an enzyme which inactivates histamine.

Its action, according to Zeller,[2] might be represented by the following equation:

$$R - CH_2 NH_2 + O_2 + H_2O \rightleftarrows R - CHO + NH_3 + H_2O_2$$

where R is an iminazole ring.

In support of this view Stephenson[3] has shown that during the activity of histaminase, oxygen is consumed and that ammonia and hydrogen peroxide are liberated. Laskowski[4] found that the amount of oxygen utilized throughout this process depends on the purity of histaminase. Among impurities affecting the enzyme haemin accelerates its activity.

There is a disagreement as to the specificity of histaminase activity. On the one hand there is a group of authors that believes it to be specific. This view was first suggested by its originators, Best and McHenry,[1] who distinguished histaminase from tyramine-oxidase. Blaschko, Richter and Schlossman[5] showed that adrenaline, aliphatic amine and tyramine oxidases are substantially similar, whereas histaminase differed greatly from them. Kapeller-Adler,[6] in one of her last works, demonstrated the difference between specific histamine-histaminase reaction and another non-specific deamination of cadaverine. Blaschko[7] showed that cadaverine and histamine had no affinity to amino-oxidase.

On the other hand, another group of authors regarded the reaction as non-specific and supposed it to be equally effective against deamines such as cadaverine and spermin. Thus Zeller, Wenk and Stern,[8] and Zeller[9] believed histaminase to be identical with deamino-oxidase and claimed also that the former produced the deamination of putrescin and agmantin.

According to Werle and Effkeman[10] and Kapeller-Adler[6] histaminase reaction is specific with regard to histamine and can only be demonstrated in serum from the pregnant woman.

There is a difference in the action of histaminase *in vivo* from that *in vitro* which was emphasized by Atkinson and Ivy.[11] Investigations *in vitro* by Kapeller-Adler[6] showed that histaminase activity was impaired in the cases of pre-eclampsia and completely inhibited by addition of aneurin.

The purpose of the present investigations was fourfold:

(1) To assess the specificity of histaminase.
(2) To estimate the activity of histaminase in non-pregnant sera.
(3) To study the fluctuation of histaminase in the course of pregnancy.
(4) To examine factors inhibiting the activity of histaminase.

METHOD.

One method of measuring the activity of histaminase employed for deamino-oxidase

and applied lately for histaminase is based upon the decolorization of indigo disulphonate presumably by hydrogen peroxide. This is the basis of the method used by Kapeller-Adler. From the degree of decolorization the activity of enzyme is estimated. Briefly the method involves the mixture of serum, histamine (cadaverine) and dye, followed by a study of colour changes. The details were as follows:

Reagents:

Solutions of:

M/15 phosphate buffer (Sorensen) pH = 7.2

M/20 histamine hydrochloride in M/15 phosphate buffer.

M/20 cadaverine hydrochloride in M/15 phosphate buffer.

200 mgms. of indigo disulphonate in 300 ml. of phosphate buffer.

The latter solution when kept in darkness for a fortnight is stable and meets the requirement of logarithmic line of the photo-electric colorimeter.

Saturated ammonia sulphate.

Acetone.

Preparation of the sera:

The sera were dialysed against the phosphate buffer in a refrigerator for 12 hours. To ensure similar conditions in all the experiments only non-haemolysed sera were used and the dialysers made in the same manner from the same material; similarly the same amount of buffer was taken for each dialysis.

To 1 ml. of dialysed serum 0.2 ml. of M/20 histamine, 0.2 ml. of dye solutions and 0.1 ml. of toluene were added. The tubes with cadaverine were similarly arranged.

Two control tubes were introduced in each of which 0.2 ml. of phosphate buffer (instead of histamine or cadaverine) was added; otherwise the compounds were the same.

Air was sucked through the mixture in each of the 3 tubes for 5 minutes. One of the two control tubes and a histamine (cadaverine) tube were set in the incubator for 72 hours at 37°C. The second control tube was put in boiling water for 2 minutes in order to stop enzyme activity, thus preventing the decolorization by histaminase.

At this juncture it seems appropriate to draw attention to 4 modifications that have been made to the original Kapeller-Adler method.

1. According to Kapeller-Adler, after 24 hours a comparison between control tube 1 and histamine tube is made thus: − = no decolorization; + = slight; + + = distinct; + + + = complete decolorization. In the present work this was modified by the addition of group ± because the distinction between minus and one plus decolorization was found difficult.

2. Air was used instead of oxygen.

3. It was found difficult to differentiate distinctly the degree of decolorization especially with the sera of early weeks of pregnancy. Therefore the time of incubation was extended to 72 hours and 12 sera were carefully studied to show the difference between 24 and 72 hourly investigations.

In Table I the results of this study are recorded. It can be seen that the 72 hours incubations gave more satisfactory results and that the decolorization of the dye in the presence of histamine as compared with cadaverine was more pronounced. Because of this histamine was chosen as a substrate and all further readings were made after 72 hours.

4. In spite of these alterations it was still difficult, because of the varying colour shades, to distinguish the degree of decolorization; this was especially noticeable in the groups labelled 'minus' and 'one plus' decolorization. To overcome these difficulties the fourth modification was introduced and an extract of dye (see below) with acetone and saturated ammonium sulphate was made. The degree of decoloriza-

tion of the dye was then measured by an Evelyn photoelectric colorimeter with filter 620, which was found the most sensitive to indigo disulphonate.

Details of Extraction.

2.4 ml. of distilled water was added to each of the investigated tubes which were then placed in boiling water for 2 minutes. After cooling for approximately 5 minutes at 16°C., 3.5 ml. of saturated ammonium sulphate and 7.3 ml. of acetone were added. Thorough shaking followed the addition of each of the above-mentioned reagents. After 15 minutes the mixture showed 3 different layers; the upper containing the dye, the middle containing the white flakes of precipitated proteins and the lower a colourless layer of saturated ammonium sulphate solution. The upper and middle layers were decanted, centrifuged at 1,500 r.p.m. for 15 minutes, when the former became a clear, transparent, bluish liquid ready for photoelectric colorimeter reading.

All galvanometer readings were converted into milligrams by means of calibration curve (see p. 489), giving the amount of dye left in the tube after decolorization. Subtracting this value from 0.133 mg. (0.2 ml. from 200 mg. in 300 ml. of buffer) which was the amount of dye originally put into every tube, regardless of the other compounds, the value of lost dye was calculated.

The calibration line was obtained as follows:

Gradually increasing amounts of dye solution were placed in 32 tubes in such a way that 4 of each of 8 different concentrations were available. Distilled water in adequate amounts was added to make up to 1.2 ml., so that proportionately volumetric changes were not made as compared with the histamine or the control tubes. The dye was then extracted as already described and average galvanometer reading for each concentration obtained. By plotting optical density (Density = 2 - log G, where G is average of 4 galvanometer readings) against the increasing amounts of dye it was clear that a straight line was a fair representation of the relationship between density and concentration of dye.

TABLE I.

Range of decolorization after 24 and 72 hours incubation at the different stages of pregnancy and with histamine and cadaverine as substrates.

Degrees of decolorization (−; ±; +; ++; +++)

No. of cases	Weeks of pregnancy	Time of incubation	Range of decolorization. Histamine	Cadaverine
2	7–9	24 hours	± to +	− to ±
2	7–9	72 ,,	± to ++	± to +
4	12–14	24 ,,	− to ++	− to +
4	12–14	72 ,,	± to +++	± to ++
5	14–27	24 ..	± to ++	± to +
5	14–27	72 ,,	++ to +++	+ to ++

RESULTS.

In the course of the present investigations it has been possible to differentiate 3 groups of factors influencing the decolorization of dye. They were as follows:

1. The diluting effect together with the many and varied properties of the serum and the loss of dye due to absorption by precipitated proteins, all of which, though

separately unknown, were present throughout the whole series of investigations.

2. The effect of incubation.
3. The addition of histamine.

On the one hand, the difference between the 1st and the 2nd control tubes (difference between point 2 and point 1) measured the loss of dye following incubation. This loss may be attributed not only to the effect of mixing serum with dye but also to factors in the sera capable of causing decolorization of dye in the absence of histamine. This amount of decolorization was arbitrarily termed "non-specific activity" of serum.

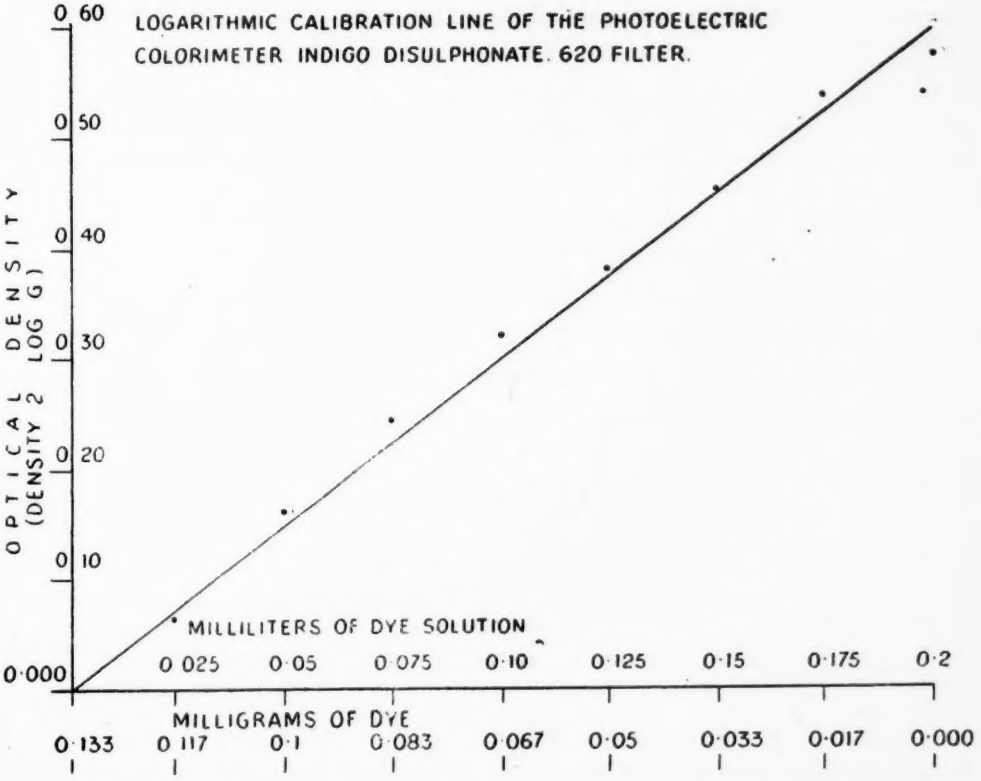
On the other hand the difference between 3 and 2 gives the measure of histaminase activity in the serum under test. This was called "specific histaminase activity."

Histaminase and non-specific activity in serum of non-pregnant women.

Investigations were carried out on 12 sera from non-pregnant women. The results are presented in Table III.

According to the modified Kapeller-Adler scale, all investigated sera have shown decolorization between – and ±. In contrast, the quantitative estimation gave the detailed value of each case in mgm. per 1 ml. Comparison between the appropriate columns (2 and 6 Table III) underlines how the latter quantitative method showed up differences which could not be demonstrated by the former, less accurate, qualitative method.

In further studies both methods were used simultaneously. Quantitative study



was carried out in order to obtain estimates of specific histaminase and non-specific activity of serum within the group of normal non-pregnant women.

It was often found with the sera of non-pregnant women, some of which had to be discarded because of uncertainty about the women's clinical state, that addition of histaminase accelerated the decolorization in one case but retarded it in another. It should be noticed in the recorded results that on 5 out of 12 occasions the values of histaminase activities were negative and no evidence of specific histaminase activity but clear evidence of non-specific activity of serum.

Changes in histaminase and non-specific activity of serum during the course of pregnancy.

The present investigations were chiefly concerned with the fluctuations of histaminase during pregnancy. The patients were chosen when the date of the last menstrual period was known so that it was possible to calculate duration of pregnancy in days.

TABLE III.

Estimation of "specific histaminase" and "non-specific" activities in sera from non-pregnant women.

Mgm. of dye per 1 ml. of serum.

No. of investigation	Modified Kapeller-Adler estimation	I Control	Histamine	II Control	Specific histaminase activity	Non-specific activity of serum
160	− to ±	0.022	0.033	0.022	0.011	0.000
167	− to ±	0.050	0.040	0.027	−0.010	0.023
169	− to ±	0.048	0.040	0.028	−0.008	0.020
170	− to ±	0.053	0.033	0.038	−0.020	0.015
181	− to ±	0.040	0.042	0.038	0.002	0.002
186	− to ±	0.052	0.053	0.022	0.001	0.030
195	− to ±	0.033	0.042	0.019	0.009	0.014
196	— to ±	0.042	0.033	0.020	−0.009	0.022
200	− to ±	0.047	0.042	0.042	−0.005	0.005
217	− to ±	0.042	0.045	0.042	0.003	0.000
218	− to ±	0.028	0.047	0.022	0.019	0.006
219	− to ±	0.031	0.043	0.022	0.012	0.009

on the remaining 7 occasions it was positive; the average was, however, very low (0.0004167, standard error ± 0.003243) and by a recognized test (Fisher[12]) was not significantly different from zero (P approximately 0.9).

In contrast, on all 12 occasions the values for non-specific activity of serum were positive and the mean (0.012167, standard error ± 0.002892) was significantly different from zero ($P<0.01$).

It could be said, therefore, that in the group of 12 non-pregnant women there was

A preliminary survey of the columns of specific histaminase activity shows a general tendency to a greater degree of decolorization of indigo disulphonate as the pregnancy advances; it could be noticed in both the qualitative and quantitative columns (2 and 6 of Table IV).

The data were subdivided into groups of equal time interval (25 days) and the average specific histaminase activity ($\bar{x}$ = mgm. of decolorized dye × 10^3) for each group was calculated together with the average duration of pregnancy in days ($\bar{t}$).

TABLE IV.

Estimation of histaminase activity. Normal pregnant sera.

Mg. of dye per 1 ml. of serum.

No. of investigation	Modified Kapeller-Adler estimation	I Control	Histamine	II Control	Specific histaminase activity	Non-specific activity of serum	Days of pregnancy
153	−	0.055	0.045	0.043	−0.010	0.012	57
124	+	0.055	0.050	0.045	−0.005	0.010	63
132	−	0.045	0.045	0.027	0.000	0.018	63
183	−	0.047	0.047	0.022	0.000	0.025	65
122	+	0.047	0.067	0.030	0.020	0.017	66
204	±	0.067	0.083	0.019	0.016	0.048	73
189	+	0.036	0.057	0.036	0.021	0.000	75
172	±	0.047	0.057	0.022	0.010	0.025	76
194	+ +	0.045	0.081	0.031	0.036	0.014	78
163	−	0.045	0.045	0.022	0.000	0.023	78
149	+	0.055	0.060	0.040	0.005	0.015	79
157	−	0.055	0.059	0.052	0.004	0.003	79
188	+	0.045	0.060	0.027	0.015	0.018	79
155	+ +	0.060	0.085	0.060	0.015	0.000	81
129	+	0.042	0.050	0.028	0.008	0.014	82
158	+	0.052	0.062	0.043	0.010	0.009	82
179	±	0.055	0.077	0.028	0.022	0.027	84
180	±	0.045	0.060	0.027	0.015	0.018	84
205	±	0.078	0.075	0.022	−0.003	0.056	85
177	±	0.050	0.072	0.027	0.022	0.023	87
211	+ +	0.040	0.057	0.036	0.017	0.004	88
99	+	0.033	0.055	0.028	0.022	0.005	94
207	+	0.060	0.093	0.020	0.033	0.040	95
137	+ +	0.062	0.072	0.062	0.010	0.000	97
152	−	0.052	0.050	0.042	−0.002	0.010	97
125	+	0.053	0.070	0.048	0.017	0.005	99
161	+ +	0.022	0.067	0.022	0.045	0.000	100
174	+ +	0.047	0.075	0.031	0.028	0.016	103
139	+ +	0.050	0.067	0.043	0.017	0.007	105
162	+	0.027	0.045	0.017	0.018	0.010	117
191	+	0.040	0.070	0.019	0.030	0.021	120
130	+ +	0.045	0.055	0.030	0.020	0.015	121
184	+ + +	0.033	0.115	0.020	0.082	0.013	133
209	+ +	0.050	0.093	0.020	0.043	0.030	139
154	+	0.052	0.072	0.028	0.020	0.024	152
175	+ +	0.022	0.065	0.017	0.043	0.005	158
178	+ + +	0.047	0.117	0.047	0.070	0.000	176
128	+ + +	0.042	0.083	0.027	0.041	0.015	182
173	+ + +	0.048	0.103	0.022	0.055	0.026	242
146	+ +	0.073	0.123	0.040	0.050	0.033	243

By the analysis of variance it was found that the variability between groups could not be explained by the variability within groups ($P<0.001$), so there can be no doubt that specific histaminase activity changes as the pregnancy advances.

The next point to be considered is the nature of the change in specific histaminase activity with advancing pregnancy. Inspection of Table IVa shows that the means of $\bar{x}$ are low in the first 100 days, thereafter rising considerably. Further analysis by the above technique showed that a straight line was not a good expression of the change. In view of the fact that there were comparatively few observations in the last few weeks of gestation the precise nature of the curve representing the change in specific histaminase activity with advancing pregnancy cannot as yet be settled. Further studies on the nature of the curve are required.

TABLE IVa.

Correlation table of the mean specific histaminase activity × 10^3 with the mean duration of pregnancy in 8 periods of gestation.

No. of observations	Days	$\bar{x}$	$\bar{t}$
6	50	3.5	64
20	75	13.85	85
6	100	26.33	111
2	125	62.5	136
2	150	31.5	155
2	175	55.5	179
–	200	—	—
2	225	52.5	242

Analysis of Variance.

	Between groups	Within groups	Total
Sum of squares	11050.61	4839.39	15890.00
Degrees of freedom	6	33	39
Mean square	1841.77	146.65	
Variance ratio	12.6		
Probability	P<0.001		

The non-specific activity of serum was similarly analyzed.

It is clear that the variability within and between groups is very similar so there is no evidence that non-specific activity of serum changes with advancing pregnancy.

TABLE IVb.

Analysis of variance.

	Between groups	Within groups	Total
Sum of squares	889.32	5603.78	6493.1
Degrees of freedom	6	33	39
Mean square	148.22	169.81	
Variance ratio	1.15		
Probability	P>0.2		

FACTORS POSSIBLY MODIFYING THE ACTIVITY OF HISTAMINASE.

A. Pre-eclamptic sera.

The sera from 9 cases of pre-eclampsia were studied as regards specific and non-specific activity of serum. In Table V the results are recorded.

It could be seen that the average duration of pregnancy in this group was longer than in our group of normal pregnant sera, so a comparison could not reasonably be made.

The means of specific histaminase activity (0.03333, standard error ±0.00557) and non-specific activity of serum (0.02867, standard error ±0.00575) were both significantly different from zero ($P<0.001$). The following guarded conclusions may therefore be drawn: pre-eclampsia does not stop histaminase or non-specific activity of serum. It is not, however, possible to say whether or not it lessens such activities.

B. Histaminase and aneurin.

Table VI presents the results from adding aneurin in the proportion of 5 mg. to 1 ml. of serum to the sera from 4 pregnant women. Sufficient serum for parallel investigations on individual samples was not available and the comparison was, therefore, made with

TABLE V.

Estimation of histaminase activity. Pre-eclamptic sera.

Mg. of dye per 1 ml. of serum.

No. of investigation	Modified Kapeller-Adler estimation	I Control	Histamine	II Control	Specific histaminase activity	Non-specific activity of serum	Weeks of pregnancy
140	+ +	0.055	0.077	0.042	0.022	0.013	33
141	+	0.085	0.100	0.050	0.015	0.035	37
142	+ + +	0.057	0.105	0.017	0.048	0.040	34
143	+ +	0.053	0.102	0.027	0.049	0.026	39
144	+	0.052	0.057	0.020	0.005	0.032	38
145	+	0.073	0.105	0.023	0.032	0.050	29
159	+ +	0.031	0.075	0.027	0.044	0.004	37
176	+ +	0.038	0.070	0.030	0.032	0.008	37
197	+ +	0.070	0.123	0.020	0.053	0.050	36

TABLE VI.

Estimation of specific histaminase and non-specific activity of serum.

Mg. of dye per 1 ml. of serum. Addition of aneurin.

No. of investigation	Modified Kapeller-Adler estimation	I Control	Histamine	II Control	Specific histaminase activity	Non-specific activity of serum	Days of pregnancy
212	−	0.085	0.090	0.030	0.005	0.055	89
213	−	0.083	0.085	0.062	0.002	0.021	96
214	− to ±	0.060	0.072	0.030	0.012	0.030	92
215	−	0.059	0.064	0.022	0.005	0.037	54

the first 26 cases of the pregnant group. In both the former and the latter series the range of duration of gestation varied between 50 and 100 days.

Qualitative estimation of sera to which aneurin was added gave negative results in 3 cases and a doubtful result in 1. Corresponding readings for sera in the group of normal pregnancies (Nos. 153 to 125, Table IV) varied between − to + +.

When the difference of the means of specific histaminase activities in the 2 groups was studied, it was found to amount to only 0.93 ($P>0.3$) times its standard error. In contrast, the difference between the means of non-specific activity of serum was 2.47 ($P=0.02$) times its standard error. In each comparison the degrees of freedom were 28.

From this analysis it could be seen that there was no clear evidence that the addition of aneurin inhibits or accelerates specific histaminase activity. The data, however, suggest that aneurin or its degradation products may accelerate non-specific activity of the serum, though the series is so small that there could be no certainty on this matter. Further investigations are required to give unequivocal results.

DISCUSSION.

This investigation presents a method for the quantitative estimation of serum histaminase which, it is hoped, will prove useful in following more precisely the changes in the amount of the enzyme during the course of normal and abnormal pregnancy.

The method was worked out from

Kapeller-Adler's test based upon a qualitative method in which H_2O_2 produced by the action of histaminase upon histamine decolorizes the dye indigo disulphonate. To this method three modifications were introduced.

1. Air was used instead of oxygen.
2. The time of incubation was extended to 72 hours.
3. The degree of decolorization was measured by an Evelyn photo-electric colorimeter (instead of naked eye distinction of Kapeller-Adler) and expressed in milligrams of dye per 1 ml. of serum.

It was found that there were 3 groups of factors responsible for the decolorization of dye. Firstly, the effect of mixing dye and serum; secondly, the non-specific activity of serum brought to light by incubation; thirdly, the specific histaminase activity resulting from the further addition of histamine. For each sample of serum 3 separate tubes were set up and studied: they were as follows: (1) serum and dye were mixed and boiled for 2 minutes to stop enzyme activity. This was called control tube II. (2) Serum and dye were mixed and incubated at 37°C. for 72 hours. This was called control tube I. (3) Serum, dye and histamine were mixed and incubated. This was called histamine tube.

In each case the decolorization was measured and expressed in mg. of dye per 1 ml. of serum. The difference between the first control tube and the second control tube is the measure of the effect of incubation upon the serum; this was arbitrarily called "non-specific activity" of the serum. This decolorization may be attributed to enzymatic reaction or oxidants present in the serum. Nevertheless there would seem to be some substances in plasma which contribute to the decolorization of indigo disulphonate and of which due account must be taken in determining the histaminase activity of plasma.

Altogether serum from 12 non-pregnant, 40 normal pregnant, and 9 pre-eclamptic pregnant women were available for this study. There was also pooled serum from pregnant women upon which the effect of adding aneurin was studied.

From the investigations upon the serum obtained from non-pregnant women there was no evidence of specific histaminase activity; but there was definite non-specific activity in the serum. The underlying explanation of the latter observation is obscure.

When, however, the serum from the normal pregnant woman was studied, there was definite evidence of specific histaminase activity. Furthermore, the activity varied with the duration of pregnancy. Thus, it was low in the first 100 days and high thereafter. These findings agree with those of others (Werle and Effkemann,[10] Kapeller-Adler[6]). Statistical analysis showed that the straight line was not a good expression of the change of this activity with advancing pregnancy. Until further cases are studied the precise nature of this change cannot be settled. The elaboration of an amine-oxidase within the body during pregnancy constitutes an interesting problem which quantitative measurement will assist in solving.

The sera from patients with pre-eclampsia showed also histaminase activity. Comparison of these findings with those of Kapeller-Adler is not easy since our data were not extensive. So far as the material allowed, it was impossible to demonstrate the inhibition of either histaminase or non-specific activities of serum.

The serum from non-pregnant and pregnant women showed roughly the same amount of non-specific activity. Furthermore, during pregnancy its amount does not change.

It was also possible to confirm Kapeller-Adler's finding that serum produces a greater degree of decolorization with histamine as a substrate than with cadaverine. A real explanation cannot yet be produced for this difference. It may represent a difference in rates of the same enzymatic reaction or be due to the presence of two enzymes.

The study of the pooled sera to which aneurin was added did not show any clear evidence that inhibition of specific histaminase activity takes place. In contrast, the data suggest that aneurin may accelerate non-specific activity of serum. Further studies on that subject are required.

It is hoped in further investigations to elaborate the function of histaminase in pregnancy. This enzyme may be an important link in the metabolism of histidine during pregnancy.

Summary.

1. The ability of serum to decolorize indigo disulphonate has been studied in 12 non-pregnant, 40 pregnant and 9 pre-eclamptic women.

2. Two important factors influenced the decolorization:

(1) Non-specific activity associated with incubation.

(2) Specific histaminase activity associated with incubation and the presence of histamine in the serum-dye mixture.

3. The evidence is presented of the existence of similar non-specific activity in sera of all three groups.

4. There was no evidence of specific histamine activity in serum from non-pregnant women.

5. There was clear evidence of specific histaminase activity in the last 6 months of pregnancy.

6. Serum from pre-eclamptic women still shows specific histaminase activity.

7. The addition of aneurin to pooled serum does not materially alter either non-specific activity or specific histaminase activity of serum though there is a faint suggestion that it may increase the non-specific activity.

8. The significance of these results has been briefly discussed.

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Acute Hydramnios

(A Brief Survey of the Recent Literature, with Report of a Case Simulating Concealed Accidental Haemorrhage)

BY

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ACUTE hydramnios is such a rare condition that F. J. Browne[1] recommends that every case should be reported. Chambrelent[2] found only 50 cases reported in the literature up to 1914, and a survey of subsequent literature reveals only a further 40 cases, making a total of 90 cases in all.

AETIOLOGY.

The cause of acute hydramnios is still unknown, and is likely to remain so until more light is shed upon the origin of the amniotic fluid and the factors which regulate the rate and amount of its secretion. Many theories of causation of the chronic variety have been advanced, and many indisputable facts have been brought forward in their support, but none of them explains why a large amount of fluid should suddenly accumulate in the amniotic sac in a matter of hours.

The amniotic fluid is generally regarded as of dual origin, being contributed both by the mother and by the products of conception. On the maternal side the fluid comes from the blood plasma, and is probably changed by its passage across placenta and amnion. The work of Polano,[3] Keiffer,[4] and Goldman[5] proved that the amnion is capable of true secretory activity.

The foetus probably contributes by urinary secretion (Acosta-Sison[6]) and by transudation from the foetal surface and umbilical cord. Under normal conditions the foetus also probably helps to regulate the amount by constant swallowing of liquor and the subsequent passage of excess fluid into the foetal circulation and across the placenta into the maternal blood-stream (Taussig[7]).

In hydramnios, therefore, pathological conditions, both on the maternal and on the foetal side (including chorion, amnion and umbilical cord), may be contributory if not sole causes of the condition.

Analysis of the 40 cases of acute hydramnios reported in the literature since 1914 reveals the following facts:

Eight cases were associated with twin pregnancy (Garipuy and Guilhem,[8] Matera[9] 3 cases, Gaehtgens,[10] Houlton,[11] Haro Garcia,[12] Audebert and Ribat[13]). In the case reported by Audebert and Ribat there was an acute accumulation of excess of liquor in both amniotic sacs. In 7 cases the foetus was anencephalic (Cornell[14] 5 cases, Payne and Bland[15] 2 cases). In the two latter cases the patients had had several previous unsuccessful pregnancies which had terminated spontaneously in the early months. Two cases were associated with teratoma of the neck (Wilson[16]).

Other foetal deformities occurring singly were: Multiple deformities (Garipuy and Guilhem[8]), atresia of the oesophagus (Fukas[17]), congenital adenoma of the lung (Esch[18]), hydrocephalic anophthalmic monster (Tillim[19]).

Maternal associated conditions found were: Ascariasis, appearing acutely in the puerperium (Lanfranchi[20]), diabetes mellitus, with recovery of both mother and child (Voron and Gaucheraud[21]).

Eclampsia—this case, like the author's, was erroneously diagnosed as premature separation of the placenta (Calatozzolo[22]).

Case Report.

Mrs. E. W., a primigravida, aged 23 years, first attended the antenatal clinic on November 27th, 1944. Her personal and family history and the history of the pregnancy were satisfactory. The previous menstrual rhythm was regular (4/28); the last menstrual period was on May 23rd, 1944, and the expected date of delivery was March 2nd, 1945. General physical examination showed a healthy, normal young woman (weight 9 stone, 6 pounds, blood-pressure 110/70; urine, sugar- and albumin-free). The abdomen contained a central tumour corresponding to the period of amenorrhoea, with palpable foetal parts and audible foetal heart. The presentation was "? vertex," and the external measurements normal; vaginal examination revealed a roomy pelvis. The Wassermann reaction was negative.

She attended the clinic again on December 18th, 1944, and was then feeling very well. She felt active foetal movements, the uterus corresponded in size to a pregnancy of 28 to 30 weeks, and the urine was albumin-free. She was told to report again for examination in two weeks.

On December 23rd, 1944, at 3.30 a.m., she was admitted to the maternity department complaining of extremely severe abdominal pain, which she said had begun suddenly on the previous evening, with vomiting. Only when the diagnosis had been established and she was closely questioned, did she admit having had vague abdominal discomfort since the previous day. The pain was constant and aching in character, and unvarying in intensity, and it was so severe that the patient retired to bed. As it persisted and she was unable to rest, she called an ambulance for admission to hospital.

On admission she looked pale and shocked and was obviously in great pain. The abdomen was extremely tense, hard and tender; occasional painless contractions were palpable. Foetal parts could not be felt and the foetal heart was inaudible. The patient volunteered the information that she had not felt any movements since the previous day. The fundus uteri reached up to about 2 inches below the xiphisternum. There was no vaginal bleeding. External ballottement could not be elicited and rectal examination revealed that the cervix was closed and not taken up. The blood-pressure was 150/90; the pulse was of poor volume and the rate averaged 150 per minute. Four ounces of urine were recovered by catheterization; it was sugar- and albumin-free.

Owing to the suddenness of onset of the pain, the hard, tense, tender abdomen, the hypertension and the poor general condition of the patient, a diagnosis of concealed accidental haemorrhage was made. Morphia gr. ¼ was administered, the blood was grouped and serum for cross-typing was obtained. The height of the fundus was marked, and the patient kept under constant supervision. At 9.30 a.m. there was no evidence of the onset of labour and the general condition of the patient was no better. The abdomen had not enlarged further but she was still vomiting. Vaginal examination revealed a closed cervix, but tense, bulging, intact membranes could be felt with the finger-tip; there was no other palpable abnormality. At this stage it was decided to try and start labour with pituitrin and stilboestrol. After 4 half-hourly doses of 0.25 c.cm. pituitrin with 5 mg. stilboestrol, pains commenced and the membranes were ruptured with a Spencer Wells forceps. It was then noticed, with considerable surprise, that the liquor was under great tension; it shot out to a distance of about 6 inches beyond the vulva. It maintained this pressure until a total of 5 pints had been collected; a further pint trickled out. The liquor was clean and normal in appearance. It now became evident that the diagnosis of concealed accidental haemorrhage was erroneous; it was a case of acute hydramnios.

The level of the uterine fundus sank down to the umbilicus and there was an instantaneous improvement in the patient's condition; she expressed great relief. The blood-pressure, which was recorded immediately afterwards, was 120/80. By vaginal examination after rupture of the membranes it was possible to feel an ear presenting; the occiput was not palpable and it was concluded

that the foetus was anencephalic. Foetal heart sounds could not be heard.

At 2 a.m. on the following day the patient delivered herself of a stillborn anencephalic foetus; this was followed 10 minutes later by the placenta and membranes.

The foetus was not macerated; it was of about 28 weeks maturity and anencephaly was the only deformity. It weighed 1 pound 2 ounces and measured 14 inches in length. There was a direct communication between the meninges and the exterior. The alimentary canal was patent throughout its length. The stomach contained about 2 c.cm. of fluid; this was not analysed. The kidneys and bladder were normal in appearance, the uterus and urethra were patent and all other organs were normally developed. The placenta weighed 5 ounces, its macroscopic appearance was normal and there was no evidence of old or recent infarcts. Microscopic section did not show any abnormality. The cord measured 9 inches in length and there were no twists or knots to suggest obstruction. The chorion and amnion were normal in macroscopic appearance. Microscopically, the epithelium of the amnion appeared less tall, more deeply stained, and less vacuolated than in the controls. The amniotic fluid was of normal appearance; unfortunately the specimen for analysis was contaminated and rendered useless.

Discussion.

Many of the cases reported as acute hydramnios cannot in fact be so regarded (if we limit the term to cases which occur within the space of a few days), though possibly they might be regarded as sub-acute. The majority of cases occur in association with some type of foetal deformity or maternal disease, which is also usually found in the chronic variety. A study of these cases also reveals the fact that in none was there very rapid accumulation of massive quantities of fluid; it was in fact the symptoms that were of sudden origin. These symptoms were not purely mechanical in origin, due to pressure, but were those of over-distention of a hollow organ, namely, pain and reflex vomiting.

Gaehtgens,[10] reporting 2 cases of acute hydramnios, both associated with uniovular twins, noted that one of the patients had received a blow on the abdomen 24 hours before the onset of symptoms, and is of opinion that this trauma was a stimulus. In the case here reported, a very careful study of the history for some weeks prior to the onset of the acute hydramnios failed to reveal any evidence of trauma, either physical or mental, and the habits and diet of the patient had not changed in any way. A striking feature, however, was the extreme spasm of the abdominal and uterine musculature. Possibly the uterine musculature of this patient was more sensitive than usual to undue stretching, and an accumulation of fluid which would ordinarily have been accommodated without much difficulty caused the muscles to go into spasm and produce the alarming symptoms. In twin pregnancy, the available uterine space is already very much encroached upon and the uterine musculature is over-stretched, so that a very little extra accumulation of liquor will be more serious.

The normal power of expansion of the uterine musculature is very remarkable, and upwards of 10 pints of fluid can often be quite readily accommodated without symptoms, except those of mechanical origin.

In this case pathological examination, both macroscopic and microscopic, of the amniotic epithelium did not reveal any evidence of acute inflammation or of any undue secretory activity. Examination of the placenta, liquor amnii and blood of the mother for syphilis and for Rh-agglutinins also proved negative. The amount of liquor was excessive, but not enough to produce pressure symptoms and not so great that it could not have been easily accommodated in the ordinary way. All the symptoms and physical signs were those

of over-stretching of the uterine musculature.

We may conclude that acute hydramnios apparently occurs in patients who would, in any case, develop hydramnios slowly, but owing to the introduction of an additional factor, namely muscle which is over-sensitive to undue stretching, especially in the presence of an extra amniotic sac, and sometimes following trauma, symptoms arise acutely.

Symptoms and Signs.

The symptoms of distension of a hollow organ will predominate rather than those of pressure; the latter will develop subsequently. Pain is the most outstanding feature. In the very early stages, the patient usually complains of an uncomfortable sensation of tightening across the abdomen; this very rapidly gives place to a very severe abdominal pain, radiating over the whole abdomen, over the sacrum, and often down the thighs. Vomiting becomes severe and persistent, often producing thirst for loss of fluid.

In the true acute variety, the signs are not those of great accumulation of fluid, but rather those of abdominal and uterine muscle spasm. The abdomen is tense, tender, and difficult to palpate; foetal parts are usually impossible to feel owing to muscle spasm, abdominal tenderness and, to a lesser degree, presence of excess liquor. The foetal heart sounds are often not heard. The degree of abdominal enlargement and the presence of ballottement will depend upon the amount of fluid, and in the true acute type these are not prominent features. The pulse-rate increases and the temperature may be raised, though usually it is not. Albuminuria is not a constant feature, and when present its quantity has no relation to the amount of hydramnios. In this case, and also in that described by Calatozzolo,[22] the blood-pressure was raised, but in the others it does not appear to have been affected. If treatment be not instituted the abdomen enlarges, signs and symptoms of pressure become more obvious, with dyspnoea, pain under the diaphragm, and oedema of the legs. Vaginal examination will reveal the usual signs of pregnancy, and if the cervix admits the tip of the finger a point of peculiar diagnostic significance will be the tense, bulging membranes.

Differential Diagnosis.

Concealed accidental haemorrhage.

Although in many textbooks this condition is not mentioned in discussing differential diagnosis, if we study the reported cases it would seem to assume first place. Calatozzolo,[22] in his case of acute hydramnios made an erroneous diagnosis of premature separation of the normally situated placenta.

Courtois[23] reported a case diagnosed as acute hydramnios which later proved to be one of concealed accidental haemorrhage. The case here described presented many features strongly suggesting concealed accidental haemorrhage —rapidity of onset of pain, vomiting and poor general condition, a tender, woody abdomen, loss of sensation of foetal movements and absence of the foetal heart sounds. The symptoms and signs are all the more misleading if there should be little abdominal enlargement and a rise of blood-pressure.

The main points of difference are: (i) the duration of symptoms—in acute hydramnios the patient, on close questioning, will often admit having had abdominal discomfort for many hours prior to the onset of acute pain; (ii) the abdominal enlargement is often, though not always, great enough to make the possibility of internal haemorrhage unlikely; (iii) ballottement, if elicited, will favour a diagnosis of hydramnios; (iv) investigation of the previous history

may help; (v) occasionally even these differential signs are absent and it is in such cases, when the diagnosis is still in doubt, that Courtois[23] recommends abdominal puncture of the uterus by a fine needle. This procedure will be required to lower the intrauterine pressure, so that nothing is lost by it. If blood-stained liquor is recovered, the subsequent treatment will be that of haemamnios. On this finding Courtois revised his original diagnosis and altered his treatment accordingly. X-ray examination will, of course, help, and should always be carried out in these cases, the presence of a foetal deformity favouring hydramnios. In the early stages of gestation it may be necessary first to establish the existence of a pregnancy. This difficulty was not met with in any of the cases described since 1914.

Other conditions mentioned in the textbooks as requiring differentiation are, occasionally, ovarian cyst, ascites and multiple pregnancy. In all the cases reviewed, the only condition which required differentiation was concealed accidental haemorrhage.

Treatment.

If the foetus is normal, an effort is made to carry the pregnancy to term. This can occasionally be achieved by frequent decompression of the uterus through the abdomen. If the foetus is deformed or the pregnancy is at term, labour may be induced forthwith. The best method is by gradually draining off the liquor by a fine needle through the abdominal wall; by this means the membranes remain intact and labour comes on slowly. The next best method is by rupture of the hind-waters with a Drew-Smythe catheter.

Acknowledgements.

The case report is presented by kind permission of Mr. St. George Wilson, Liverpool Royal Infirmary. The sections of placenta and amnion have been reported upon respectively by Professor Davie, University of Liverpool, and Dr. A. B. Bratton, London County Council Central Histological Laboratory, to both of whom my thanks are due.

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Treatment with Penicillin of Some Obstetric Cases

BY

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THE following account of the use of penicillin presents illustrations of its value in cases of sepsis in obstetrics. The patients, who were all treated at the County Infirmary, Carmarthen, consisted of 5 cases of Group A haemolytic streptococcal infections of the genital tract with complications, and 2 cases of bullous impetigo in neonates.

The 5 cases of streptococcal infection were first treated with sulphanilamide. The routine dosage employed was 2 g. initially, a further 2 g. in 4 hours and then 1 g. 4-hourly. This treatment was started as soon as there was rise of temperature or pulse-rate. Bacteriological examination was immediately carried out on vaginal, nose and throat swabs, and a catheter specimen of urine. Penicillin treatment was started only when it became clear that the infection was not being controlled by sulphanilamide.

CASE 1.

Mrs. A. D., aged 35, a 5-gravida, had nothing relevant in her previous obstetric history. She was admitted at term as an emergency on September 12th, 1944, in the first stage of labour. There was a history that the patient had been in bed at home for a fortnight before admission with pyrexia and a left facial palsy. On admission to an isolation ward her temperature was 102.6°F. and her pulse-rate 120 per minute. Her general condition was poor; there was a left facial palsy and a dry, fibrosed perforation of the left tympanum. Other abnormal physical signs were not found. Her labour was uneventful and she was delivered naturally of a healthy infant an hour later. Sulphanilamide therapy was started immediately and bacteriological investigations were carried out. The temperature settled the morning after delivery but the pulse-rate remained at 100 per minute. The bacteriological examination showed a heavy growth of Group A haemolytic streptococci in the vagina alone (the ear swab being among the negative findings). On September 14th (2nd day of puerperium) the patient's abdomen became distended and she developed generalized abdominal tenderness. Her general condition deteriorated. A provisional diagnosis of general streptococcal peritonitis was made, and the abdomen was opened the same day through a small low median incision. There was some serous exudate and the small bowel was distended. The exudate was aspirated and on direct culture grew Group A haemolytic streptococci. A tube drain was left in the abdominal wound for 3 days. On September 15th, as there was still further deterioration in the patient's general condition, penicillin therapy (15,000 units 3-hourly) was started and the sulphanilamide discontinued. The pulse-rate began to settle the day after penicillin was started. It was given for 4 days and then stopped. The haemoglobin level on September 18th was 52 per cent and the patient was given a transfusion of 2 pints of fresh blood.

There was a further rise of temperature and pulse-rate on September 22nd, and again on September 25th, when penicillin (15,000 units 3-hourly) was restarted for another 4 days. The temperature and pulse-rate again settled—this time in 3 days. At this stage the patient became fractious and was difficult to manage. She objected strongly to the pain of the penicillin injections and discharged herself against advice on October 2nd, the 20th day of the puerperium. Her general condition was then fairly good, the abdominal wound was healed and the facial palsy improved.

She was readmitted a fortnight later (on October 17th) with a history of intense headaches, vomiting, drowsiness and pyrexia for the previous

week. She was now running a remittent pyrexia. There was bilateral papilloedema with a patchy retinitis and a left facial weakness. The abdomen did not show any abnormality. The cervix was healthy, the uterus well involuted and the appendages normal. Routine bacteriological examination did not show haemolytic streptococci in the vaginal swab. Lumbar puncture revealed a normal cerebrospinal fluid. She was transferred to Oxford under the care of Mr. J. Pennybacker as a possible cerebral abscess. Investigations at Oxford showed that she had a cerebral thrombophlebitis. From October 26th to November 8th she had a further 1,900,000 units of penicillin at Oxford. She returned to Carmarthen on November 18th and went home on the 21st in good health.

Comment. There is considerable evidence that the sulphonamides have reduced the incidence of general peritonitis as a complication of streptococcal infections of the genital tract. Streptococcal peritonitis still has a high mortality even with sulphonamide therapy. It remains to be seen whether or not the use of penicillin—as illustrated above—will be a more effective form of treatment. In this particlar case the initial course of penicillin was undoubtedly too short (penicillin at the time was difficult to get for civilian use).

CASE 2.

Mrs. H. M. L., a primigravida aged 26, was admitted on September 12th, 1944. She was a florid, obese patient who had hypertensive toxaemia throughout her pregnancy. She was admitted at the 38th week because of the sudden appearance of oedema and albuminuria in addition to the long-standing hypertension. In view of this and of the fact that her sister had had postnatal eclampsia 2 years previously, labour was induced by sweeping and rupturing the membranes after premedication. She had a spontaneous delivery of a live infant. An hour later she had an eclamptic fit and was given 500 c.cm. of 40 per cent glucose intravenously and morphia gr. ½. She had 7 more eclamptic fits within 12 hours, was given more morphia and intravenous glucose and 1 pint of blood was withdrawn by venesection. She eventually settled down 15 hours after delivery.

On September 16th (4th day of the puerperium) she developed a temperature of 99.5°F. with a pulse-rate of 136 per minute and was isolated. Sulphanilamide was started. The vaginal swab showed a very heavy growth of Group A haemolytic streptococci. On the 7th day of the puerperium her temperature rose to 103°F. with a pulse-rate of 120 per minute. She developed abdominal distension and generalized abdominal tenderness. The abdomen was drained the same day through a small lower median incision. Fluid taken from the abdomen at operation did not grow any organisms, but fluid taken from the drainage tube 3 days later grew haemolytic streptococci.

The temperature began to show signs of settling, but rose again to 101°F. on September 26, and a vaginal swab on that day still showed a very heavy growth of Group A haemolytic streptococci. Sulphanilamide therapy was continued and repeated white-cell counts were done. On October 7th, after 21 days of sulphanilamide, came the first warning of agranulocytosis. The white cell count on that day was 4,550 per c.mm. with 30 per cent polymorphs and 51 per cent lymphocytes. The sulphanilamide was discontinued and Pentnucleotide (40 c.cm. daily and Vitamin C (600 mgm. daily) were given. Daily white cell counts showed gradual deterioration and on October 10th the total white cell count was 3,400 per c.cm. with only 4 per cent polymorph neutrophils and 1 per cent basophils.

In view of the facts that the patient still had a heavy streptococcal infection, that she was deprived of her natural cellular defences and that further treatment with sulphanilamide was dangerous, penicillin therapy was started on October 10th. The patient was given 15,000 units 3-hourly and this was continued until the white cell count returned to normal on October 17th, by which time the temperature and pulse-rate had also settled. Between October 10th and 17th the patient was also given alternate daily transfusions of 1 pint of fresh blood, daily parenteral liver ("Examen" 4 c.cm.), in addition to the Pentnucleotide and Vitamin C.

After October 17th the patient made steady progress. She had developed a superficial thrombophlebitis in the left leg on October 15th, which

gradually subsided. She was discharged in good health on November 10th. Postnatal examination on December 14th revealed a blood-pressure of 145/80, and a healthy pelvis.

Comment. In this case the general peritonitis had subsided before penicillin was started. It was the onset of a severe agranulocytosis with the heavy streptococcal infection persisting in the genital tract that provided the indication for penicillin. Superficial thrombophlebitis is a not uncommon complication of penicillin therapy.[1]

CASE 3.

Mrs. W.B., a primigravida aged 32, was admitted on October 30th, 1944, and had a normal delivery of a full time infant. On the 3rd evening of the puerperium she developed a temperature of 103.6°F. and a pulse-rate of 120 per minute. She was isolated and given sulphanilamide therapy. Routine bacteriological examination showed a very heavy growth of Group A haemolytic streptococci in the vagina. The temperature and pulse settled gradually, but on the 10th day of the puerperium both rose again (temperature 101°F. to 102°F.; pulse 120 a minute). The temperature and pulse settled again in another 4 days, and on the 17th day the sulphanalimide was discontinued.

On the 24th day of the puerperium there was another sharp rise of temperature to 104.6°F. and of the pulse-rate to 136 per minute. The vaginal swab on that day still showed a heavy growth of haemolytic streptococci and sulphanilamide treatment was restarted. On the 25th day of the puerperium the white cell count was 6,000 per c.cm. with only 39 per cent polymorphs. Sulphanilamide was discontinued and penicillin (15,000 units 3-hourly) was given together with Pentnucleotide, 40 c.cm. daily. The Pentnucleotide was stopped after 3 days and the pencillin after 5 days. The pyrexia and rapid pulse-rate settled the day after penicillin therapy was begun. The clinical appearance of the patient improved rapidly and she was discharged in good health on December 5th; the 37th day of the puerperium. Postnatal examinations on December 23rd showed a healthy cervix, a uterus well involuted, and normal appendages.

Comment. The indication for penicillin in this case was similar to that in Case 2. The only difference was the degree of agranulocytosis.

CASE 4.

Mrs. E. A. J., aged 33, a 6-gravida, was admitted in labour on March 23rd, 1945, as a case of pre-eclamptic toxaemia. She was at term, her blood-pressure was 170/90, the urine was loaded with albumin and there was oedema of the legs. She had a spontaneous delivery. On the 3rd day of the puerperium she complained of a sore throat, had a temperature of 101.5°F. and a pulse-rate of 110 per minute. She was isolated and given sulphanilamide. Routine bacteriological investigations showed a very heavy growth of Group A streptococci in the vagina alone. On the 3rd day of treatment the haemoglobin was 50 per cent and the patient was transfused with 1 pint of fresh blood. There was no improvement after 6 days and penicillin was started. Both temperature and pulse settled on the following day. Penicillin was continued for another 5 days. On April 7th, 2 days after it was stopped, the temperature and pulse rose again. The left leg became oedematous and painful and there developed a clear picture of femoral thrombophlebitis. Bacteriological examination on April 7th did not show any haemolytic streptococci in the vaginal swab. Further penicillin was not given. The haemoglobin level was still only 64 per cent on April 8th, and a further transfusion of 1 pint of concentrated red cells was given. The thrombophlebitis subsided without incident, and the patient was discharged in good health on May 25th. Postnatal examination on that day showed an old laceration of the cervix, a well involuted uterus, and normal appendages.

Comment. Clinical response to sulphonamide therapy was not evident after 6 days, and on this indication penicillin was started with striking effect.

CASE 5.

Mrs. F.O., aged 23, a primigravida, was admitted on September 28th, 1944, at the 39th week of a twin pregnancy for pre-eclamptic toxaemia. Labour was induced by sweeping and rupturing the mem-

branes and live infants were delivered without incident. On the 4th day of the puerperium she developed a temperature of 103°F. and a pulse-rate of 130 per minute. She was isolated and given sulphanilamide. Routine bacteriological examination showed a very heavy growth of Group A haemolytic streptococci in the vagina. She ran an intermittent pyrexia which settled on the 12th day of the puerperium and she discharged herself against advice on the 13th day (October 14th).

She remained at home in indifferent health and 3 weeks later she became acutely ill and was readmitted to hospital on November 7th. On admission she had a temperature of 104.8°F. and a pulse-rate of 128 per minute. She complained of a great deal of pelvic pain. She had a large, tender, fixed mass in the right side of the pelvis and the uterus was pushed over to the left. Penicillin (15,000 units 3-hourly) was started at once. The temperature was normal the next day but the pulse-rate was still high—118 per minute. The same day (November 8th) the pouch of Douglas was explored by a posterior colpotomy. Pus was not found and a small de Pezzer tube drain was left in the incision for 3 days. The fluid from the tube was sterile and the vaginal swab grew coliform bacilli only. The pulse-rate gradually settled and the temperature did not rise again. The pelvic mass gradually resolved, and during its resolution it became more and more obvious that it was a parametritis. Penicillin was stopped after 7 days. A striking feature of this case was the marked improvement in the clinical condition of the patient effected by penicillin in 1 week. She was discharged on November 27th in good health. Postnatal examination on December 16th revealed a healthy cervix, the colpotomy wound healed, and the uterus, parametrium and appendages all normal.

Comment. The swift response to penicillin suggests that the parametritis, which followed a streptococcal genital tract infection, was due to a penicillin-sensitive organism. The swabs from the de Pezzer tube drain and the vagina were taken 20 hours after penicillin was started. It is possible that the negative swab findings may have resulted from this amount of penicillin therapy.

CASE 7.

Infant B. was born on July 23rd, 1944. The delivery was at term and was normal. On July 27th the baby developed bullous impetigo—first in the folds of the neck and eventually over most of the body. Swabs showed a very heavy growth of *Staphylococcus aureus*. At the time there was an outbreak of bullous impetigo in the nursery. The affected infants were isolated and their lesions and cord stumps were dusted with sulphathiazole powder. The ruptured bullae were dried before the powder was applied. Most of the infants responded to this treatment. In the case of Infant B the lesions kept on spreading and red indurated areas developed round some of them. Penicillin ointment was applied after 8 days of sulphathiazole powder and the condition began to subside. The ointment was applied 8-hourly, and the lesions were cleared in 6 days. The infant's general condition was much improved.

CASE 8.

Infant J., born on July 29th, 1944, was a similar case. Penicillin ointment was applied to the lesions after 3 days initial trial with sulphathiazole powder. The rash cleared in 7 days.

Comment. Staphylococcal bullous impetigo has been a troublesome infection in nurseries in the last few years. Its control has been thoroughly investigated recently.[2] Penicillin ointment, properly prepared[3] and handled, offers a simple therapeutic measure well worthy of further trial.

CONCLUSIONS.

In the cases described the patients were very ill. The first 2 patients, in spite of early sulphonamide-treatment, developed peritonitis. In Cases 2 and 3 sulphonamides were pushed to the stage at which agranulocytosis developed—a complication as dangerous as the original infection. Before penicillin was available there was no further line of treatment, and it is probable that Case 1, and possible that Cases 2 and 3, would have died. The rapid

improvement with penicillin was therefore all the more striking.

The cases are few in number and it will be some time yet before the value of penicillin can be fully assessed and compared with that of the sulphonamides.

My thanks are due to Drs. R. M. Fry and J. M . Boissard of the Emergency Public Health Laboratory, Carmarthen, for the bacteriological work and for their active interest and guidance, and to Professor Miles H. Phillips for his clinical help and advice.

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A Case of Meigs's Syndrome

BY

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LAWSON Tait[1] described a condition in women in which he found both ascites and hydrothorax. He did not think that these findings were always pathognomonic of cancer and even at that time advised laparotomy in such cases. The presence of ascites, hydrothorax and an ovarian fibroma is well established as a syndrome bearing the name of Meigs[2] since he and his colleagues first recognized this triple condition. Gardiner and Lloyd-Hart[3] estimated the number of reported cases as 38, including 1 of their own. Since this publication, Clay *et al*[4] in Britain have published 2 more. Kehidai[5] in Hungary has added another and with the case described below the total is now 42. By far the majority of cases have been reported from America.

CASE REPORT

H.K., 26 years old, resident in Istanbul, 9 years married, 1 child 7 years old, was admitted to 2nd University Obstetric Clinic on May 31st, 1943. She complained of abdominal swelling and breathlessness which had started 9 months before. In the previous winter she had been treated for pleurisy. Menstruation had always been regular.

Clinical examination. The patient, of average build, had cyanosis of the face and dyspnoea. The heart was shifted to the left but the sounds were normal, pulse 108, blood-pressure 135/90. There was a right pleural effusion. The abdomen was distended with fluid and in the hypogastrium was a hard and irregular tumour, the size of a foetal head. On vaginal examination the uterus could be felt normal in size but lying behind the tumour. Urine was normal. *Blood*: Haemoglobin 86 per cent (Sahli), erythrocytes 5,000,000; leucocytes 10,400 (differential count—eosinophils 1 per cent, polymorphs 74 per cent, band forms 2 per cent, lymphocytes 20 per cent, monocytes 3 per cent). Sedimentation rate (Westergren) ½ hour, 8 mm.; 1 hour, 52 mm.; 2 hours, 90 mm.

Diagnosis. A solid tumour of the ovary with ascites—fibroma or carcinoma. In view of the pleural effusion, consultation with a physician was arranged. The pleural effusion was considered to be an aftermath of the attack of pleurisy during the previous winter.

Treatment. Conservative treatment was advised by the medical specialist—low salt diet, calcium, vitamin C, cardiac tonics. Fig. 1 is a radiogram of the chest taken on June 5th, 1943. On June 21st 1,200 c.cm. were aspirated from the pleural cavity. The fluid was serofibrinous, dark yellow, Rivalta positive, density 1915, albumin 6 g. per litre, erythrocytes and leucocytes were present. Fluid was found at the same level in the pleural cavity (Fig. 2) the day after the aspiration and dyspnoea had returned. On July 5th a second aspiration (2,000 c.cm.) was performed. Two days later a further radiogram was taken and the fluid was found at the old level. In view of the persistence of the effusion, the marked dyspnoea and the orthopnoea it was decided to do a laparotomy.

Laparotomy (July 19th, 1943). Just before the operation 2,750 c.cm. of fluid were aspirated from the pleural cavity. Spinal anaesthesia (5 c.cm. of 2.5 per cent novocain solution) was used. An ovarian tumour was removed and also 2 litres of blood-stained fluid.

Pathological anatomy. The tumour was solid with a thin capsule, the cut surface showed whorls of fibrous tissue. Cystic spaces were absent. Histologically there was no lipoid and no epithelium but the tissue was rich in cells. Diagnosis—fibroma of ovary.

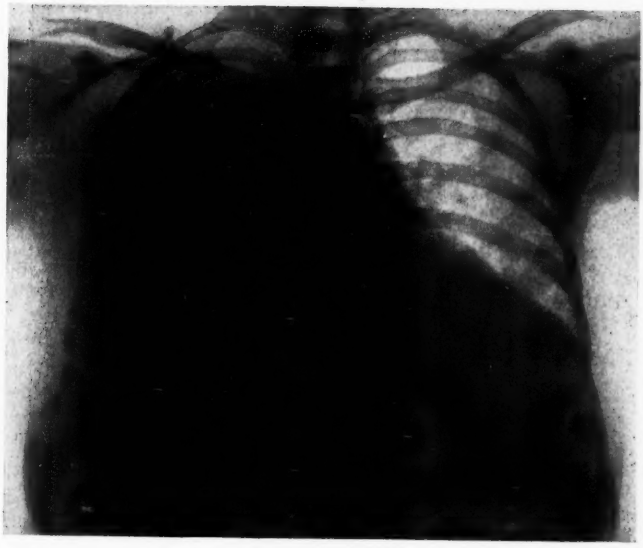

FIG. 1.

Before aspiration.

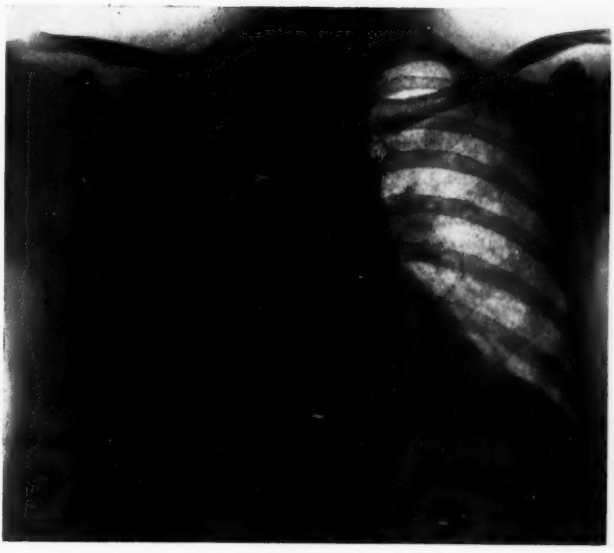

FIG. 2.

One day after aspiration.

N.E.

Carcinoma of the Female Urethra

(Review of the Literature and Report of Three Cases.)

BY

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MY interest in carcinoma of the female urethra was stimulated after encountering 2 cases in a year, and a third case that occurred in the same Emergency Medical Service Sector is added. The cases are not of themselves especially noteworthy, although the condition is a rare one, but this review is presented as there has not been any recent account in the British literature. Boivin and Dugès[1] first recorded a case of carcinoma of the female urethra in 1833, and subsequently Menville[2] collected 149 cases (up to 1935). Many of the reported cases are incompletely described, and in particular histological details are often missing. Another difficulty is that in advanced cases the disease spreads widely, so that it may not be possible to demonstrate its site of origin with certainty; and conversely vulvovaginal growths may invade the urethra.

Urethral carcinoma appears to be commoner in the female than in the male; Nichol[3] stated that 149 cases had been reported in males and 262 cases in females. The true incidence of carcinoma of the female urethra is difficult to establish. Hamann and Göbel[4] found that it accounted for 0.16 per cent of gynaecological carcinoma, but Menville[2] found only 1 instance among 43,000 gynaecological cases. Sarcoma of the female urethra is still less common, only 22 cases having been reported.

Etiology. Urethral carcinoma is usually a disease of the postmenopausal woman, the average age in 109 cases being 53 years (Menville[2]) but it is seen in younger women, as for example Watson's[5] patient, aged 27.

In the male, urethral carcinoma frequently follows stricture or fistula (Scholl and Braasch[6]), but in the female predisposing factors are less definite. The disease is mostly seen in parous women, and following Ehrendorfer[7] most authors have mentioned trauma or chronic inflammatory processes as etiological factors. Hallé[8] claimed that leukoplakic changes could be discovered in the urethra in cases of carcinoma, but I have not found any confirmation of his observations, and, so far as the vulvo-urethral type of growth is concerned, this is an unlikely event, for the vestibule is usually exempt from the changes of leukoplakic vulvitis. Urethral caruncle is sometimes suspected to be a predisposing lesion, but in view of the frequency of occurrence of caruncle, it is hard to be sure that the supposed relation is not merely that of chance. In the second case below, some evidence is brought forward to suggest that malignant change may occasionally occur in a caruncle, though it is not suggested that it is a common event.

I have looked through the notes of 82 cases of caruncle and examined most of the sections, but cannot find other clinical or histological suggestion of any relation between caruncle and carcinoma, though 4 of the caruncles were recurrent.

Pathology. Following Winckel, Whitehouse[9] divided the cases into urethral and

vulvo-urethral types, and the latter are found about twice as often as the former. Whitehouse's account of the gross pathology is still one of the most valuable, and it is difficult to add much to his description:

A. Urethral carcinoma. This is seen in two common forms: (1) In the usual form the growth appears as a malignant ulcer in the urethral floor, most often in the distal urethra. (2) The less common form is that of periurethral induration, extending for some length along the urethra, and ulceration is late.

B. Vulvo-urethral carcinoma presents in 3 forms: (1) A vascular papillomatous nodule at the posterior margin of the urethral orifice. (2) A nodule that breaks down to an ulcer in the vestibule. (3) A scirrhous induration around the urethral orifice.

On microscopical examination the neoplasms are found to be of varying type, but the lack of exact histological data in many of the reports makes exact statistical statement impossible. Squamous cell carcinoma, columnar cell carcinoma (both simple and adenocarcinoma), mucoid carcinoma, and undifferentiated types all occur. In most series squamous cell carcinoma predominate. The following figures are based on the reports of Menville,[2] Nichol,[3] Watson,[5] Scholl and Braasch,[6] Whitehouse,[9] Palmer,[10] Pugh,[11] Pomeroy,[12] Menville and Counseller,[13] Sparks and Parsons,[14] Sala and Levine,[15] Tuta and Hess,[16] as these cases are all fully reported, and the present cases are added. Among 27 cases of urethral carcinoma there were 12 cases of squamous cell carcinoma, 10 of columnar cell carcinoma (4 of these were adenocarcinomata), and 5 of undifferentiated carcinoma. Among 42 cases of vulvo-urethral carcinoma there were 31 cases of squamous cell carcinoma, 9 of columnar cell carcinoma, 1 of mucoid carcinoma, and 1 of undifferentiated carcinoma. In the whole series 64 per cent were squamous cell carcinoma.

Menville[2] has stressed the similarity of the growths to neoplasms of the bladder. It is also suggested that the well differentiated adenocarcinomata may arise from the paraurethral glands, but this statement is conjectural rather than proven. The squamous cell neoplasms appear to be radiosensitive, but evidence is incomplete about the other types.

Clinical features. Urethral carcinoma does not produce much discomfort in the early stages, and, even after severe symptoms appear, patients so commonly delay seeking advice that extension to bladder, vagina or lymph nodes may have already occurred by the time the patient is seen.

Perhaps the commonest of the early symptoms is painful micturition. In some cases, particularly of the sclerosing type of growth, difficult micturition or retention may occur; in other cases, frequency. Bleeding is a common symptom, more especially with micturition, but, in the case of growths projecting from the urethra, at other times also. Local tenderness and dyspareunia also occur with the more superficial growths. Some of the patients may report a swelling in the region of the urethra, or even in the groin, when inguinal metastasis has occurred. The symptoms naturally vary with the type of neoplasm; the papillomatous vulvo-urethral type chiefly causes haemorrhage and pain, in the ulcerating types pain is the chief symptom.

On examination the growth may be seen projecting from the urethral orifice, or in other cases may be felt *per vaginam* as a line of induration along the urethra. Enlarged inguinal glands are found in about 20 per cent of cases at the first examination, though the enlargement may be due to secondary infection of the growth rather than metastasis. (It should be noted

that the lymphatics of the upper urethra also drain into the intrapelvic nodes). Biopsy is the final and essential step in diagnosis, sometimes with the aid of urethroscopy.

Treatment. Shaw[17] has published a full review and no new principle can be added to his general account. As regards the primary tumour the choice between surgical excision and irradiation is obviously affected by the position and extent of the growth. If the posterior urethra is involved the growth can be excised only at the cost of permanent incontinence, although this can occasionally be overcome by suprapubic drainage if the bladder can be closed below (Battle[18]) or by ureteric transplantation. Irradiation has less operative risk, although there is a possibility of both fistula-formation and stenosis. The radiosensitivity of the growth varies with its type, and although it is generally stated that the squamous cell types are sensitive, there is less agreement about the columnar cell types. Radium needles can be inserted from above through the bladder as well as from below, if necessary. Radium has often been chosen for the more advanced cases, and this should be remembered when comparison with surgical results is made. The greater number of recent authors have preferred irradiation for the primary growth, employing interstitial radium, but the best plan would seem to be to treat each case individually, using irradiation for the more extensive growths, particularly of squamous cell type, and excising early growths, particularly those of the lower urethra. As biopsy is commonly necessary it would seem reasonable to excise a small tumour complete, rather than to remove a small part of it.

As regards the inguinal glands there is the same choice between surgical excision and irradiation, and here there is fairly general agreement that surgery offers the best results. The nodes are often infected, and the overlying skin may not tolerate the large doses of radiation necessary to reach the glands in their fatty bed. Taussig[19] has strongly advocated the Basset type of operation, even if the lymphatic nodes do not show clinical evidence of involvement.

It is difficult to draw definite conclusions about the choice of treatment from the literature, as the accounts given are so often inadequate, and also because of the short periods of follow up. Although individual accounts of success by many different methods can be found, the results in general are disappointing. Sparks and Parsons,[14] for example, found only 15 survivors out of 119 after 3 years. Taussig's[19] results are among the best, and his figures are especially valuable as they are based on an accurate follow up over 5 years. He reported 14 cases, and in 2 of these the disease was too advanced for treatment. Of the 12 cases treated 8 were treated by irradiation, with only 1 survival; 3 cases were treated by excision of the primary growth with Basset gland dissection, and all 3 survived; 1 other case was unsuccessfully treated by local excision alone.

Case Reports. Some apology is necessary for presenting these 3 cases, as the criticisms that I have made of other reports apply in part to mine, particularly as 1 case was followed for only 2 years. Furthermore, 2 cases were treated at a period of the war when radium was not available, and radon was used somewhat unscientifically.

CASE 1.

A widow, aged 73, who had borne 1 child and had 1 miscarriage. Menopause at 50. She complained of bleeding " from the vagina " for 2 years. There had not been pain or urinary symptoms. On examination a soft vascular rounded tumour, 2 to 3 cm. in diameter, with a nodular surface was found attached to the posterior margin of the urethral orifice, and a deep submucosal extension was

spreading to surround the orifice. Soft inguinal glands were palpable, but not larger than are commonly felt. On October 3rd, 1941, the tumour and the adjacent tissues including the lower half of the urethra were excised, and it was possible to bring the mucosal edges together. Six radon seeds of 1.3 mc. were implanted around the operation site, and a catheter left in place. Bilateral dissection of the inguinal glands was performed.

Microscopical section showed an undifferentiated epidermoid carcinoma, with the cells arranged in large syncytial masses separated by scanty stroma. In other areas the cells were arranged more loosely presenting an appearance mimicking that of sarcoma. The hyperchromatic cell nuclei showed many mitoses. Most of the tumour was acutely inflamed and infiltrated with polymorphs. The inguinal lymph glands showed chronic inflammatory changes without evidence of metastasis.

After the operation the vulva and right leg became oedematous, but this soon subsided. The patient remained well for 2 years, but trace of her was then lost as she left London and did not answer letters.

This was a highly malignant and undifferentiated carcinoma and it is of interest that parts of the section mimicked sarcoma, though the growth as a whole was clearly a carcinoma, as a similar difficulty in diagnosis has been reported by Menville.[2]

CASE 2.

A widow aged 70, who had 3 children. Menopause at 47. She complained of bleeding at the end of micturition, for 2 weeks. There were no other symptoms. Five years previously a urethral caruncle had been removed. On examination an almost spherical vascular tumour 2 cm. in diameter was found at the posterior margin of the urethral orifice, and extending upward slightly into the canal. The mass was tender, firm in consistence, with a slightly nodular surface. Soft glands were palpable in both groins. Other pelvic abnormality was not found. On May 21st, 1941, the tumour was excised with a ½ cm. margin of tissue, and 8 radon seeds of 1.3 mc. each were implanted around the operation site. It was possible to oppose the mucosal edges, and a catheter was left in place. The patient was frail, and in view of her age inguinal dissection was not performed.

The microscopical section showed tissue composed of fibrous and granulation tissue, with marked superficial inflammation. There was extreme hyperplasia of the overlying stratified epithelium with marked activity of the cells suggestive of an early epithelioma, with infiltration at one point. The decision to leave the inguinal glands was supported by the relatively benign and early appearance of the growth.

The patient remained well for 3 years, but later in that year a local recurrence appeared, and she was admitted to Lambeth Hospital where she was treated with X-rays and by implantation of radon seeds, with retrogression of the growth. In April 1945 (4 years) there was no further evidence of recurrence.

This case was one of a very early squamous cell carcinoma, occurring at a site from which a caruncle had been removed 5 years previously. Although the tumour was 2 cm. in diameter, and presumably had been present for some time, the greater part of it consisted of granulation tissue, and the carcinoma itself was evidently very recent, possibly supervening on a pre-existing caruncle.

CASE 3.

This patient was under the care of Mr. A. J. Heriot and Mr. J. H. Peel and I am grateful to them for allowing me to include her. She was a parous woman aged 82, gravely ill on admission. She complained of pain in the lower abdomen and back of 1 week's duration, and of constant dribble of urine with haematuria. On examination the bladder was found to be distended up to the umbilicus, and attempts to pass a catheter failed because the distal urethra was surrounded by a submucous induration, which extended beneath the intact vaginal epithelium. The inguinal lymphatic nodes were not enlarged. Suprapubic drainage was established, and part of the growth excised for section.

The section showed sheets of carcinomatous cells, with a good deal of variation in size and shape, but mostly definitely squamoid, although without prickles or cell nests.

Fifty mg. of radium in a flat container with screenage equivalent to 3 mm. of lead was applied to the anterior vaginal wall and vestibule for 48 hours on 2 occasions. The growth retrogressed so that a catheter could be passed, but the patient's general condition remained precarious, and she died a month later. Permission for a postmortem examination was not obtained.

SUMMARY.

The literature on carcinoma of the female urethra is reviewed. Three new cases are reported.

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Fused Twin Monster

BY

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THE incidence of double monsters is low and the statistics of their occurrence are not particularly accurate. Mall[1] states that 7 per cent of all pregnancies terminate in aborted pathological ova and about 0.6 per cent in malformed foetuses at term; of the latter only a small proportion are conjoined twins. Puech[2] in 100,000 births found 517 malformations of various sorts, but of these only 2 were double monsters. Adair[3] reported 2 double monsters in 25,000 deliveries at Chicago Lying-in Hospital. Mudaliar[4] reported 4 double monsters between 1920 and 1928 among 25,000 deliveries and Rydén[5] 2 thoracopagi in 40,000 births at Lund, Sweden, between 1900 and 1933. These figures can be compared with the rate of monozygotic twins which comprise 25 per cent of all twins; the ratio of all twins to single births being 1 to 85.2.

Joined-together twins may be described as human beings that have more than enough parts to make 1 individual, but not enough parts to make 2. Newman[6] states that one-egg twins are the product of an incomplete twinning division symmetrically placed with respect to each other, i.e., one has developed from the right half of an embryo and the other from the left half. They are almost exact mirror-image duplicates. Double monsters are very rarely born alive because of the mechanical difficulties of delivery. "Siamese" twins are 2 nearly complete individuals and are therefore less monstrous, and cases of survival have been reported. The teratogenesis of the united twins has excited much interest and discussion; Ballantyne[7] is inclined to accept the theory of polyspermy as the determining cause of these monstrosities. If two fertilizing spermatozoa gain entrance into the ovum, 2 primitive streaks, each with its own orientation, may be looked for; the proximity or separation of the primitive streaks will determine the relation of the future twins. The streaks may be in opposition to each other, when the craniopagous type of double monster may result; they may lie side by side, when thoracopagous twins will be produced; or they may be inclined towards each other at their anterior or posterior ends, when syncephalic or dicephalic terata will be formed. In all these monstrosities the twinship is the essential and original pathological fact.

CLINICAL HISTORY.

Mrs. H.S. was 19 years old when she attended this antenatal clinic with her first pregnancy. Her general health had always been good and there was nothing relevant in her past history. The last menstrual period was stated to be about August 18th, 1944, making the estimated date of delivery May 25th, 1945. She had married after conception occurred.

On examination she was seen to be anaemic, but other organic abnormality was not detected. The urine was free from abnormal constituents and the blood-pressure was 122/70. The pregnancy appeared normal for the period of amenorrhoea

until the 5th month. The pelvis was roomy. Between the 5th and 6th months the uterus became very tense and distended with numerous foetal parts. A provisional diagnosis of multiple pregnancy was made. Undue discomfort was not noticed until the 36th week, when she became dyspnoeic, had difficulty in getting about and developed mild toxaemia. She was admitted to hospital on May 4th, 1945. At this time there was generalized moderate oedema, a trace of albumin in the urine and the blood-pressure was 160/110. The abdomen was enormously distended and it was impossible to make out anything definite as hydramnios was present. An X-ray examination was carried out and the following report given: "Multiple pregnancy; twins; ? triplets; 2 presenting by the vertex; leading head appears deformed; ? dead foetus. Impossible to get a satisfactory A.P. view because of hydramnios. There are shadows in the lateral film which would do for 3 spines."

The toxaemia improved with rest in bed, but in view of the enormous abdominal distension and the fact that labour had not begun by June 2nd (1 week overdue by dates), the membranes were ruptured artificially and 5 pints of liquor amnii allowed to escape. The presenting part was very high and thought to be a face or anencephalic foetus. Four hours later good, regular contractions started and liquor drained abundantly from the vagina. On abdominal examination at this time doubt was felt as to the diagnosis of multiple pregnancy, as the whole abdomen was now soft without any apparent second bag of membranes. Limbs were easily palpable all over the abdomen, but a definite head could not be felt anywhere. A vague suspicion of fused twin monster was entertained, and it was decided to carry out a thorough vaginal examination after several hours of labour, as the pelvis was very roomy. The cervix, however, dilated very rapidly, and 6 hours after the onset of labour pains it was fully dilated with what appeared to be a face presentation just inside the vagina. Under anaesthetic a full examination was made and showed a double face, with chin anterior, and an underdeveloped cranial vault. The forceps were applied and a fairly easy extraction of the fused anencephalic faces was achieved, with the aid of an episiotomy. The shoulders were difficult to deliver and the posterior arm was first brought down. Traction was then applied together with fundal pressure during the pains, the rest of the monster being delivered with ease.

The placenta was single and infarcted with only 1 set of membranes; it measured 9 inches in diameter. A moderate postpartum haemorrhage was controlled by oxytoxic drugs and a hot intrauterine douche. The patient made a good recovery.

The fused twin monster was stillborn and weighed 8 pounds, the sex being female. See Figs. 1, 2 and 3.

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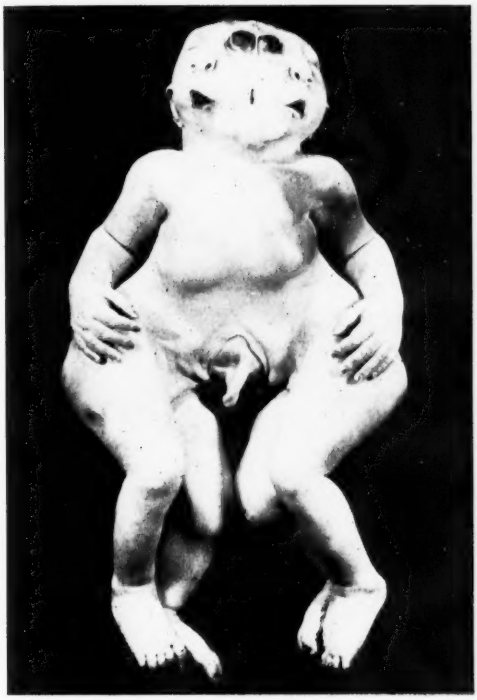

FIG. 1.

N.L.K.

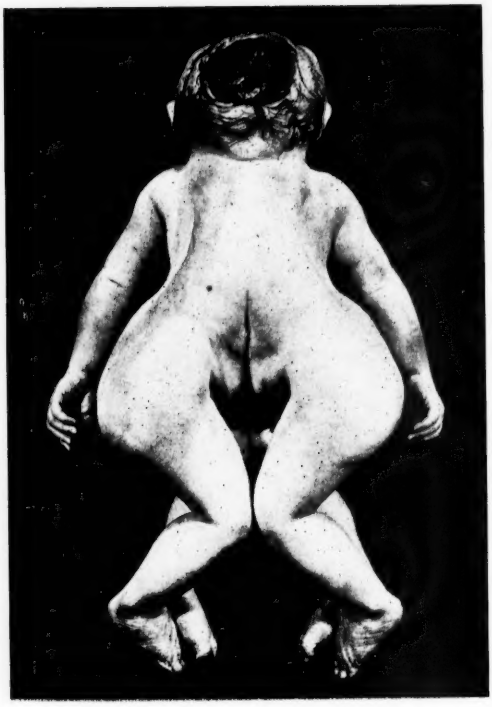

FIG. 2.

N.L.K.

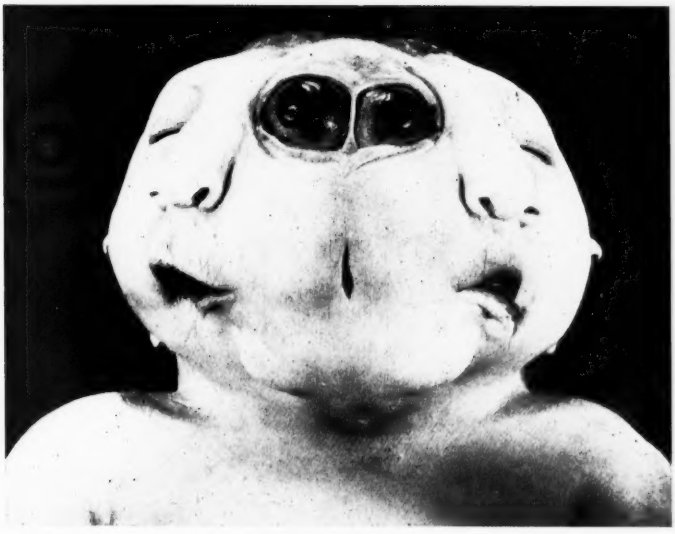

FIG. 3.

N.L.K.

A Case of Sympus Dipus

BY

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SYMPUS dipus, or symmelia, is a foetal abnormality, characterized by the almost complete union of the lower extremities, and terminating in a double foot, the sole of which is turned to the front. In view of its constancy in almost all cases of sympus, and only in this type of monster, one other characteristic feature may be added, that is, as was first pointed out by Behn[1] in 1827, the presence in the umbilical cord of 1 vein, and a single artery.

Proshek[2] in 1925 was able to collect from the literature only 10 authentic cases of true sympus dipus reported since the year 1800, and described a case which occurred in the private practice of Dr. Fred L. Adair in 1923. Dreyfuss[3] reported another case of this type in 1928, since when no other has been recorded.

The rarity of such a foetal malformation, and the tendency for such a foetus to adopt the breech position, makes the following case of interest.

A healthy primigravida, aged 24 years, visited the antenatal clinic for the first time when she was 16 weeks pregnant. The family history revealed the presence of 1 set of twins, a brother and sister, 2 years younger than the patient. There was no other significant fact in the history. On physical examination the uterus was found to correspond with the duration of amenorrhoea. The Wassermann reaction was negative, and the urine and blood-pressure normal.

An abnormality was not detected during the antenatal period until the 32nd week, when a breech presentation was palpated, the foetal head being easily ballotted in the right hypochondrium. External cephalic version was attempted, but this was unsuccessful, owing to deep engagement of the breech in the pelvis. The patient was asked to come into hospital for version under anaesthesia on the following day. However, labour commenced prematurely, and an easy spontaneous delivery occurred 7½ hours later. The foetus, which weighed 3 pounds 15 ounces, and was 17 inches long, was born with its fused lower extremities extended over its abdomen, and died soon after delivery.

The foetus presented the following unusual features:

The lower extremities were completely united as far down as the toes, and were in a position of complete extension, a position which was maintained after delivery (Plate I). In the region of the knee joints, there was a faint linear depression, indicating the line of fusion of the limbs. Two femora, and two patellae were felt, the latter being directed postero-laterally, a small dimple on the right side marking the medial margin of the right patella.

The heels were fused and placed anteriorly, as were the plantar surfaces of the fused feet. Six toes were present, 3 on each foot. The external genital organs were not present, and there was no anal opening. The umbilical cord contained 1 vein and a single artery, which was found to communicate with the aorta directly, before its bifurcation.

X-ray examination showed 2 femora, and 2 fibulae on the inner aspects of the tibiae (Plate II).

Autopsy disclosed absence of the kidneys and ureters, marked distension of the lower gut, which appeared to enter a rudimentary bladder, that is, a persistent cloaca. A testicle was found on each side, in the inguinal canal. The upper extremities, chest, and head were normal.

This foetus hence exhibited all the classical features of true sympus dipus, according to the classification of St. Hilaire.[4]

Commentary.

St. Hilaire[4] in 1836 first classified foetal abnormality of this type according to the extent of the union of the lower extremities into the following groups:

(i) Symèle, in which the lower extremities are almost perfectly united, and terminate in a double foot, the sole of which is turned to the front.

(ii) Uromèle, in which the lower extremities are very incompletely united, and terminate in a double foot, usually very incomplete, the sole of which is turned to the front. According to Bennington,[5] the limb may contain 3 bones, sometimes 2, and only 1 patella. In this class of foetus there is neither anus nor urinary tract. The external genital organs are usually present.

(iii) Sirénomèle, in which there is incomplete fusion of the lower extremities, which terminate in a stump, or in a point without a distinct foot. Bennington describes the foot as sometimes being represented by a toe, or rudiment of a toe.

Förster[6] in 1861, introduced a classification, similar to that of Hilaire, merely altering the terminology, which is now generally used in the English literature. The symèle of St. Hilaire he called sympus dipus, the rarest of this type of foetal abnormality. The uromèle was called sympus monopus, and the sirénomèle sympus apus, the commonest form of sympus according to Proshek.[2]

Aetiology.

Four main theories are put forward to explain the causation of sympus dipus:

(1) Weigert[7] and Kampmeier[8] assert that the single artery in the umbilical cord is present in almost all cases of sympus, and only in this type of foetal monstrosity. They therefore conclude that this anomaly was the primary cause of such an abnormality. Weigert further believes that the fusion of the limbs and associated maldevelopments are only secondary, due to malnutrition as a result of impaired blood supply.

(2) St. Hilaire[4] and Solger[9] explain the fusion of the limbs by an approximation of the side plates from which the limbs are developed and as a result of that approximation, fusion takes place. St. Hilaire based his theory on the law of affinity of "like for the like." That is, the union was what he called a "natural" process, quite as natural a process as the union of other parts of the body, which at first lateral and paired, afterwards become united. The reason why the extremities do not as a rule unite, was because they do not have the opportunity of coming into contact.

(3) Gebhard[10] and Gruvillier,[11] adopt the view that fusion occurred as a result of pressure, either by the amnion or by the uterus itself.

(4) Bolk[12] explains these monsters as being due to "mechanical" disturbances in the germ plasma.

Diagnosis.

In no case was sympus dipus suspected before delivery in the cases mentioned above. In all but 1 case, hydramnios, which is usually expected in the presence of foetal malformation, was not present.

PLATE I.

Breech Delivery. Sympus Dipus.

Note—Absence of rotation of hind limbs. Non-development of external genitalia and absence of anus.

L. R.

PLATE II.

L. R.

In a case of twins associated with hydramnios, described by Bauereisen, the first foetus presented all the features of true sympus dipus, the second infant showing atresia of the anus and rectum, the bowel ending blindly in the posterior wall of the bladder, and absence of one kidney. The cases reported by Bauereisen,[13] Gladstone,[14] Proshek,[2] Dreyfuss,[3] and in this paper, were delivered as breech presentations. Details of the mode of delivery in the remaining 8 were not mentioned.

It appears therefore that the only aid to the diagnosis of such foetal monstrosities before delivery, is the location of the fibulae on the medial aspects of the tibiae, on radiological examination.

Summary.

A case of sympus dipus is described, and the theories of causation outlined.

A possible aid to the diagnosis before delivery is suggested.

I wish to thank Mr. George Brown, Medical Superintendent to this hospital, for his permission to publish this case, and Sister Winters for the clinical photographs.

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BOOK REVIEWS

"The Premature Baby." By V. MARY CROSSE, M.D., D.P.H., M.M.S.A., D.R.C.O.G. 1945. 156 pages. Published by J. & A. Churchill, Ltd., London. Price 10*s*. 6*d*.

AFTER reading this book, one wholeheartedly reiterates the views of the writer of the foreword: "This book is unique in British literature."

By producing enlightening statistical tables the author adds weight to her invaluable suggestions for the reduction of mortality and morbidity among these babies. There is no doubt that it is the co-operation between obstetricians, paediatricians, general practitioners and midwives on the lines clearly indicated in this book which will help to bring about the reduction we desire.

Especial stress is laid on the dangers of infection. The value of penicillin is now apparent. Its lack of toxicity compared with the sulphonamides makes it often the drug of choice in the treatment of infections in premature babies, and this should be stressed in a subsequent edition.

More recent work appears to contradict the author's statement that the absence of immune agglutinins in the serum of a Rh negative mother carrying a Rh positive foetus means very little. We now know that in these cases the agglutinins may be fixed by the foetal blood. Again, there is now evidence that even hydrops foetalis may be compatible with survival if the infant is transfused at birth.

However, these are the only criticisms, constructive in intent, that can be made of a most valuable book whose widespread use is strongly recommended.

A. H. C. WALKER.

"Diagnostic Methods Used During the Later Months of Pregnancy and During Labour." (Fifth edition.) By J. C. WINDEYER, M.D., Ch.M. (Sydney), M.R.C.S. (England), L.R.C.P. (London), F.R.A.C.S., F.R.C.O.G. Professor Emeritus, late Professor of Obstetrics, The University of Sydney. 1945. 32 pages. Sydney: Australasian Medical Publishing Co. Ltd. Price 2*s*.

IN this little book there is no attempt made to cover the subject of antenatal care. The purpose is to make the reader familiar with the bedside methods of examination to be used in late pregnancy and labour—viz. abdominal, vaginal and rectal examination and pelvimetry.

As might be expected emphasis is laid on abdominal examination. The best part of the book is that dealing with palpation of the abdomen. This is described in six steps:

(1) The recognition of the foetal back.
(2) Palpation of the anterior shoulder.
(3) To verify the diagnosis of the position of the head.
(4) To estimate the degree of flexion of the head.
(5) Estimation of the relative size of the head and the pelvic brim.
(6) Estimation of the approximate size of the foetus.

Palpation of the anterior shoulder, and estimation of the relative size of the foetal head and the pelvic brim are particularly well done. The course taken by the anterior shoulder in anterior and posterior positions receives careful consideration. The value of accurate shoulder palpation as a means of estimating progressive descent of the foetal head on the one hand, or arrest of descent on the other, is clearly described.

X-ray pelvimetry receives a brief mention. It is stated that this will become the rule rather than the exception in the near future. While the reader is reminded that one cannot foretell how the head will mould or how strongly the uterus will contract during labour, mention is not made of the necessity for *first class* radiological standards and accuracy, if this kind of pelvimetry is not to be misleading.

When discussing ausculation the author omits to point out that in extended breech presentation, with the breech deeply engaged, the maximal intensity of the foetal heart is to be found *below* the umbilicus.

Vaginal examination is described at length. Smooth gloves are advocated as causing the least discomfort and trauma, and diminishing the risk of carrying infected material upwards. Digital estimation of pelvic conformation, and the assesment of cephalopelvic proportion or disproportion, are described at length. But the necessity for the bladder being empty before this is attempted is not mentioned. Yet even Caesarean section has been performed unnecessarily because of such an omission.

Exception might be taken to the unqualified statement that rectal examination is without risk to the mother.

This little book is well worth reading. It is the attempt by an able clinician to inspire the attainment and maintenance of a high standard of clinical examination. Other special methods are relegated to their proper place—adjuvants to the clinical approach. It can be recommended to all who practise or wish to practise the obstetric art.

ANTHONY W. PURDIE.

" Human Embryology " (Prenatal Development of Form and Function). By Professors W. J. HAMILTON and J. D. BOYD, and Associate-Professor MOSSMAN. 1945. 345 pages. Cambridge: Heffers. Price 31*s.* 6*d.*

BOOKS on human embryology have two uses: either to provide a reader with an account of the present state of our knowledge of human development and its relation to general biological principles; or to provide a medical student with as much of those matters as is of value to him in his studies and practice. It is the opinion of the writer of this review that it is impossible for anyone to write a book to serve both these ends successfully. A book which satisfies the first reader is one with full details of the subject, written in such a manner that comparison with other mammals or vertebrates is easy, with an ample bibliography and an assumption that the reader has already taken a course of comparative embryology and is conversant with the technical terms and practical methods connected with the subject. For, after all, no one thinking to begin to study embryology seriously would start at the mammals. Before we can see how a textbook of embryology should be written for the benefit of those studying medicine, we must first decide the place the subject occupies in the curriculum, and, if we really face facts, we come to these conclusions. Certain facts of the subject are part of the essential knowledge of all general practitioners of medicine; the knowledge of certain others are part of the necessary mental equipment of various specialists; but the great bulk of the facts of human development have no permanent value to a graduate of medicine and many of them never have any value at all.

The subject is included in the course of anatomy because: (*a*) it explains the reasons for many facts of adult structure and therefore makes them easier to remember; (*b*) it explains many abnormalities which the student is bound to meet in the dissecting-room or operating theatre; (*c*) it makes the whole lay-out and structure of the body more intelligible and the study of it, therefore, more intelligent. Besides this it is educational, training one's visual memory and powers of three-dimensional visualization, as well as being informative and instructive on a subject which should be intensely interesting to anyone wishing to take up a medical career. But, with the exception of the facts mentioned above as part of the necessary equipment of a trained medical man, the subject is not included in the curriculum for its own sake, is not taught to students with a basic knowledge of vertebrate embryology and is not learnt so that students may become embryologists. In these circumstances a textbook of Human Embryology should be written in the plainest English, with the minimum of technical terms and scientific names which appertain only to embryology, and with no more detail than is consistent with truth and a sufficient presentation of the subject; sufficient, that is, to allow it to play the part in the curriculum indicated above.

Now it must be obvious that no book can be written to satisfy the needs of both these types of readers, because what is necessary for the first one makes the book unsuitable for the second. The book of which this is a review, however, attempts to satisfy both, and, as a result, will satisfy the student of embryology; but includes a chapter on Comparative Vertebrate Embryology, which he

will not find very useful. On the other hand, the medical student will find the bulk of the text overloaded with technical terms, language and detail, and containing much that will tend to hinder rather than help him. Considering the early stage in his university career at which he studies the subject, a glossary and a fuller index would have greatly added to the value of the book to him. The authors do not seem to have realized sufficiently how wide is the difference between their own learning and language and the knowledge of a second-year medical student, but, if they thought it necessary to write in such technical language and to introduce so many technical terms, they should have made it as easy as they could for the reader to find out the accurate meaning of the words used. (A word like "congenital" should be carefully defined whereas its meaning can only be incorrectly gleaned from the explanation given of "congenital disease." The introduction of the word "herniates" by putting it in brackets after the word "projects" and then the omission of any index reference to the page is another example.) The present reviewer, however, is one of those people who perhaps has a bee in his bonnet over what some writers call "jargon", and another might not be appalled by the fact that, in a very fully illustrated book of 345 pages, technical words or phrases are stressed by being printed in italics not far short of two thousand times.

But apart from these criticisms, which some people will not consider to be very serious, there is little but the highest praise to be given to the authors and their collaborators. The book is the most complete, the most splendidly illustrated, and, thanks to the inclusion of the findings of experimentalists, the most alive account of human development to date. I very much doubt whether a textbook of embryology will ever be better illustrated than this one: it is not simply that Mr. A. K. Maxwell is a master of his art and craft, but that the authors have appreciated how supremely important illustrations are and how numerous and well-chosen the figures must be to enable those unfamiliar with the subject fully to understand the text, however clearly that may be written. The text in this volume is, when one considers the amount of detailed information it contains and the complication of the subject, extraordinarily lucid and easy to read; and, altogether, the authors are to be congratulated upon having produced a most valuable book and a most acceptable addition to any biological or anatomical library. It is as good as it well could be for a student of embryology who wishes to read a full and up-to-date account of the state of our knowledge of human development and well worth the guinea and a half (a very reasonable price for such a book even before the war) to a medical student, if only for the illustrations with which it is so abundantly adorned.

G. L. PURSER

"Control of Pain in Childbirth." By CLIFFORD B. LULL, M.D., F.A.C.S., and ROBERT A. HINGSON, M.D., with a Foreword by NORRIS W. VAUX, M.D. 1944. 356 pages. Philadelphia, London and Montreal: J. B. Lippincott Co. Price 7.50 dollars.

THIS volume of some 300 pages is, like most American publications, handsomely produced and beautifully illustrated with photographs and coloured diagrams. Perhaps this aspect of the book is overdone, for example, it is hardly necessary to use a full-page coloured diagram (Plate VII) to illustrate that in caudal anaesthesia the needle may be properly placed in the caudal canal or improperly placed in the periosteum or outside the sacrum.

The book opens with an excellent account of the anatomy of the nervous system and of the pelvis and its organs, and the pharmacology of various anaesthetic and analgesic agents. The bibliography is immense, and therefore as a book of reference the volume may be commended. But if the purpose of the authors, as one is led to believe, is to sift all the evidence and present it in a practical form, then I think there is something left to be desired. From the mass of material presented it would be difficult for anyone without wide experience to assess the value of any one method. Its claim, therefore, to be an aid to the general practitioner is doubtful. Indeed the general practitioner in reading the list of apparatus necessary to control pain in home delivery may wonder why the only item omitted is the pantechnicon to convey it all.

The chief interest of the book is the account of caudal analgesia which is claimed to be the greatest advance so far in the control of pain in childbirth. It is claimed that in 40 to 60 per cent of cases the

force, frequency and duration of uterine mobility are not altered; but in nulliparae, because of loss of muscle power, low forceps will in most instances have to be applied. In 20 to 25 per cent uterine tone is diminished but the amplitude of contractions increased. In both these groups labour is said to progress rapidly and the level of analgesia does not proceed above the 9th thoracic segment. But there is a third group in which there is diminution of the amplitude of contractions, and in which, we are told, the analgesia may reach the 5th to the 1st thoracic segment; labour is ineffectual, and there is foetal (not to say maternal) anoxia!

The technique of administering caudal analgesia would be difficult and time-consuming enough in hospital practice where there is every facility for assistance and a good aseptic technique, but it is difficult to believe that it can be widely adopted in general practice unless the patients can afford the whole-time attendance of an anaesthetist and obstetrician, or, shall we say, an obstetrico-anaesthesiologist.

A great part of the work would appear to be a treatise more on obstetrics than on anaesthesia. In a book purporting to discuss the control of pain in childbirth is it necessary to list Stroganov's theories on eclampsia, or the caution necessary in the selection of donors for Rh negative patients? And surely the section on X-rays of the sacrum and pelvis is outside the problem of anaesthesia. In the coloured photographs illustrating the actual birth of a child by natural or surgical means the mother is shown laughing appreciatively and wide-mouthed, unscreened from the field of operation; also, 75 per cent of her attendants have their noses uncovered! The style is a little verbose and sentimental and the book adds up as a textbook of obstetrics written by an expert in the use of caudal analgesia.

DOROTHY SPENCE SALES.

REVIEW OF HOSPITAL REPORT

THE CLINICAL REPORT OF THE NATIONAL MATERNITY HOSPITAL, DUBLIN, FOR THE YEAR 1944.

DURING the year there were 3,858 patients admitted to the maternity wards of the hospital. There resulted from these 3,187 intern-deliveries. This is an increase of 168 admissions and 185 deliveries on the previous year's figures. The result, according to the Master, is an overloading of the intern maternity service with the resultant evils of the shortened puerperium and incomplete establishment of breast feeding. As the number of beds in the maternity department is not stated it is not possible to estimate just how serious the overcrowding is.

In the first 17 pages there is a summary of the most important features of the report. The next 73 pages are concerned with detail. Here many conditions are set out case by case while others (e.g. breech delivery and delivery by the forceps) are summarized numerically in tabular form. Why these conditions should be selected for compression is not made clear. It is to be regretted in breech presentation. A distinction is not drawn between complicated and uncomplicated breech. The foetal mortality (3 stillbirths) in primigravid breech presentation (19 cases) is stated to be 15 per cent. What interests the obstetrician is the foetal mortality in uncomplicated primigravid breech delivery. This figure is obscure. But if we exclude 2 cases delivered by Caesarean section and 3 " associated with twins," then we have 3 stillbirths in 14 breech deliveries, i.e., 21 per cent.

Of 83 cases of persistent occipito-posterior position 29 were delivered by the forceps, 10 of these as unreduced posterior positions. Brow presentation deserves special mention. There were 8 (not 7 as stated) cases of brow presentation. All 8 were delivered by the vaginal route with 6 living infants (2 infants were stillborn, but in each case the forceps had been applied unsuccessfully before the admission of the patient to hospital): there was no maternal death.

There were 4 cases of pubiotomy or symphysiotomy. Dr. Spain is convinced that these operations have a small but definite sphere of usefulness. He does not enlarge upon the indications for their use, but draws attention to the pelvic architecture of the subjects in which they were employed. In 3 the main feature was a narrow pelvic outlet. This indication is stressed by others who still find a limited place for these operations. In the 4th case there was narrowing of the mid cavity of an asymmetrical pelvis, due to inward bulging of an acetabulum. (Spelling in this section is rather eccentric.)

There were 17 cases of destructive operations on dead infants to facilitate delivery. These were mainly perforation of the foetal head. It is not made clear whether any difference is implied between " perforation of the head " and " craniotomy." There were 6 elderly primigravidae in this group and 4 of these had severe toxaemia. Caesarean section might have been preferable treatment. We are not told, however, which cases were "booked" and which were "emergencies" ("admitted at term in labour " might fall into either category.) It is difficult, therefore, to evaluate the line of treatment followed. There is no specific statement on the maternal result, save that 3 cases were morbid. While the presumption is that none died, the statement that 3 were morbid would be equally true if the 3 had died (B.M.A. standard).

There is a more liberal use of Caesarean section than formerly. There were 64 (not 63 as stated in the tables) cases of first Caesarean sections (including hysterectomies). It is stressed that all were lower segment sections. An arbitrary limit is not set to the number of repeat sections which can be carried out on the same individual provided they are lower segment operations, performed by

competent operators under good conditions. This view has allowed the more liberal use of the operation in the elderly primigravida, placenta praevia, toxaemia (for which 8 sections were performed), and certain other obstetrical conditions. There were 29 (not 30 as stated) "repeat" sections. There was 1 maternal death in the 93 cases. Except in a few cases of placenta praevia, the anaesthetic used for all sections was local infiltration with 0.5 per cent novocaine with, in addition, sufficient nitrous oxide and oxygen to allay the patient's anxiety. While there were no stillbirths, there were 8 neonatal deaths. In 5 of these the section was done for placenta praevia—in 3 (not 4 as stated) the child weighed less than 5 pounds. It is interesting to note that even though there were 5 neonatal deaths in the 20 cases of placenta praevia delivered by Caesarean section, in 10 cases of placenta praevia treated by Braxton-Hicks or internal version only 1 child survived.

The placenta was removed manually on 45 occasions. Most practising obstetricians would agree with the Master that, when haemorrhage is present, this is a simple and effective operation, provided it is done promptly while the patient's condition remains good. Doubtless the Master is equally right in his criticism that the blood transfusion situation in Dublin is unsatisfactory. In the only death in this series the removal was undertaken for retained placenta with postpartum haemorrhage. The patient did not have a blood transfusion. The cause of death was shock and haemorrhage.

The hospital morbidity on the B.M.A. standard is 1.78 per cent.

There were 17 maternal deaths. These are set out clearly in a table of some 6 pages. Four of these might be classed as 'avoidable'—1 case of puerperal sepsis in which many attempts at delivery before admission had failed; 1 of central placenta praevia when Caesarean section might have been preferable to Braxton-Hicks version and the bringing down of a leg; 1 rupture of uterus which occurred (in a case undergoing trial of labour) while preparations were being made for Caesarean section; and the case of postpartum haemorrhage already referred to, when blood transfusion might have saved her.

Brief reports follow on extern maternity cases, the infants', the gynaecological, the X-ray and the pathological departments.

This is not an easy report to read. The 17 pages of the summary are clear and interesting, but the tables of detailed cases make heavy reading. So much matter is contained under "remarks" that "summary of the case" would be a more accurate description. In spite of their being so long, information which would be of value is sometimes omitted, e.g., the degree of dilatation of the cervix when prolapse of the umbilical cord was first diagnosed. It seems undesirable to record in the tables under the heading "Result M.C." 'L' for a child which in fact died. An example of this is seen on page 45, Reg. No. 20850. Glancing quickly down the table it would seem that the result to all the children on that page was favourable. Only after reading a "remark" approximating to 40 words do we find out that the child whose "result" was said to be 'L' actually died. Why not record the result as 'N.D.' or 'Died' where it can be seen at a glance.

Even if somewhat heavy reading this is a most interesting report. Here we see reflected the outcome of vital thought. In this year's work we find the altering attitude to the elderly primigravida, placenta praevia, the severe toxaemia and Caesarean sections. That this is not mere change for the sake of fashion is to be gathered from Dr. Spain's remarks (page 16) on the subject of induction for suspect disproportion in the primigravida.

ANTHONY W. PURDIE.

Obituary

James Hendry

1886—1945.

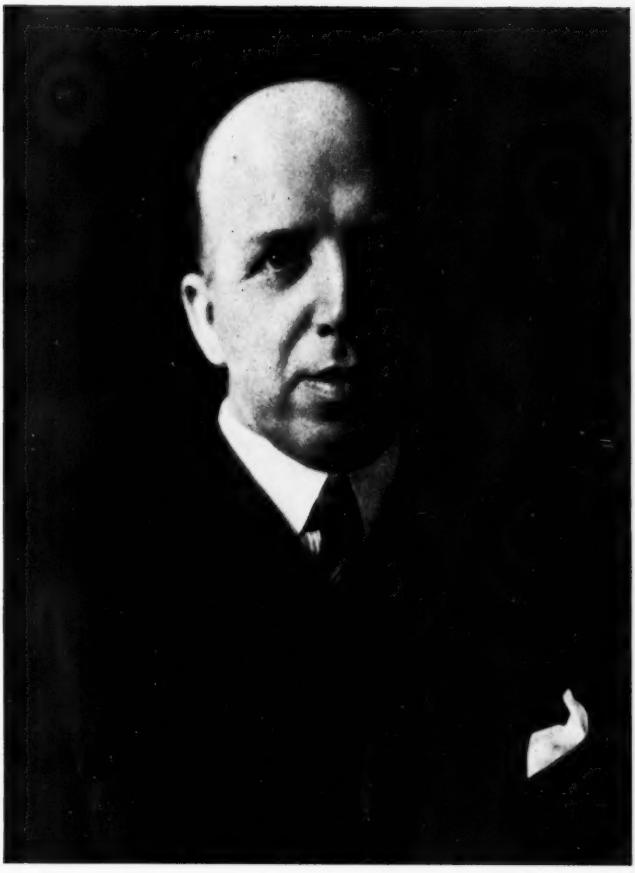
THE death of James Hendry at the comparatively early age of 59 came as a grievous shock to his colleagues, and to his many friends and former pupils.

Hendry's qualities of character—simplicity, honesty of purpose, integrity and industry—were obvious; and you were not long in his company before his many-sided ability unfolded itself, and aroused ever-increasing appreciation and respect the more you got to know him. Not without these great qualities would his fellow undergraduates of Glasgow University have voted him into the Presidential Chair of the Students' Representative Council, and colleagues of later years have nominated him to serve on "The Interdepartmental Committee on Medical Schools" (Goodenough Committee). Such distinctions are not easily attained.

Reference to Hendry's undergraduate days would not be complete without a mention of his long services in and for the O.T.C. of Glasgow University. In the earlier months of the Great War of 1914-18 he was first captain and later adjutant of the Corps. In 1916 he went out to France and served as major with the R.A.M.C. until demobilization.

Hendry's entrance into the speciality of obstetrics and gynaecology was by an unusual route. He never did any spell of service as house physician or house surgeon in medical, surgical, or obstetric wards. He came direct to my department—introduced to me by my then senior assistant, now Dame Louise McIlroy—from Professor Noel Paton's Physiological Laboratory, where he occupied the post of Muirhead Demonstrator. When I talked over the question of his transference to my department Noel Paton was laudatory as regards Hendry's ability; but he remarked that if I could get any writing out of Hendry it was more than he could ever accomplish. Curiously enough this particular dislike of writing persisted all through his professional life as my co-authors of the "Combined Textbook of Obstetrics and Gynaecology" can attest. By some, possibly by many, this may be accounted to him for righteousness in these days of literary verbosity and outpourings of pseudo-scientific "research." But in Hendry's case it was unfortunate because he, by reason of his extended scientific training in physiology and his post-graduate studies in the clinics of Germany and France—he spent close on 2 years abroad—had something to contribute that no other to a like degree possessed. Special mention should be made of the months he worked in the Clinique Tarnier, Paris, where he made contact with Professor Paul Bar whose investigations in antenatal physiology are even to-day recognized as of the highest quality.

Hendry's greatest literary contribution to our speciality—and it is of outstanding merit—are the chapters on the Physiology and Pathology of Pregnancy in "The Combined Textbook of Obstetrics and Gynaecology." When written for the first edition,



JAMES HENDRY

published in 1923, they were singled out by many critics for special praise. It was his purpose in the next and 5th edition—he took over the editorship from me shortly before his death—to rewrite these chapters. Now the authors will find it most difficult to fill his place, for on these particular subjects few can write with the same assurance as Hendry could.

Hendry was the perfect chief-of-staff. During the 8 years he was my first assistant and Donald MacIntyre was second, with Norman Cruikshanks and later Dougal Baird our registrars, the unit was singularly well organized and efficient. This naturally continued after he succeeded me in the Muirhead Chair at the Royal Infirmary, and took on Dougal Baird as his chief assistant. Like all great leaders Hendry selected his assistants with the greatest care.

Following on his appointment to the Muirhead Chair in 1927, and as the years passed, his natural gifts in administrative work—early manifested when he was first Secretary and later President of the Students' Representative Council—came to be recognized by his colleagues in the Senate. After serving a period as Dean of the Medical Faculty he went on to be its representative on the University Court. And his activities extended into ever-widening fields and pastures new. He was Chairman of the Medical Committee of the Scottish Advisory Committee of the Nuffield Provincial Hospitals Trust, and a member of the Medical Advisory Committee to the Secretary of State for Scotland. He also served for many years on the Council of the Royal College of Obstetricians and Gynaecologists. And, as already mentioned, he was chosen to represent Obstetrics and Gynaecology on the small and very important "Interdepartmental Committee on Medical Schools," under the chairmanship of Sir William Goodenough. The report of this Committee, known as the "Goodenough Report" appeared in 1944.

In the obituary notices in the *Glasgow Herald*, of September 10th, are the words—"Dr. Hendry's capacity for work was always a marvel to his friends and associates. Every hour of the day was filled with teaching or operating or administrating. When he was not in committee, in the classroom or in the operating theatre, he was travelling by night to London to give his services in wider spheres."

Hendry's transference to the Regius Chair, which occurred in 1943, furnished him with the opportunity to carry out a scheme which for long had been in his mind—to make the Regius Chair a "whole-time" unit with the Royal Maternity Hospital the clinical centre for obstetrics, and the gynaecological wards at the Royal Infirmary the clinical centre for gynaecology. What was in his mind was to create a large maternity and gynaecological unit for undergraduate and postgraduate teaching comparable with the famous Rotunda Hospital in Dublin. His personal sacrifice to this statesmanlike scheme was to give up his very large consulting practice. Untimely death deprived him of witnessing the evolution of what would have undoubtedly been, under his direction, one of the greatest centres for obstetric and gynaecological undergraduate and postgraduate teaching in the British Empire.

In any walk of life—church, bar, army, politics, commerce—Hendry would have attained a distinguished position. Circumstances, but more probably choice, directed his energies very particularly along administrative lines. This, however, he in no way allowed to interfere with his duties as professor and as practising specialist in obstetrics and gynaecology. He was a most efficient and inspiring teacher in the classroom and at the bedside; while in debate, by reason of his academic gifts, clarity of

thought, and power of exposition he had few equals.

The President of our College, Eardley Holland, in the gracious tribute he paid to Hendry's memory in the columns of *The Times*, described him as "One of these rare people who with truth might be said to have no duplicate." Possibly he attempted too much—especially during the years of war—and thereby overtaxed his physical powers, great as they were. But this was inevitable! With Hendry the motive and driving power of all his activities were a high sense of duty and of service. Sir Hector Hetherington, Principal of Glasgow University, in a moving address at the memorial service held in the University Chapel on September 12th, refers to this in words which could not be more feelingly or gracefully expressed: "He had great natural gifts—tireless energy, a wide, exact and beautifully ordered memory, so that he could bring to bear on any situation the full range of his experience and knowledge, a cool and balanced judgment, executive skill of the highest order. And with these, kindness, patience, good humour, forthright honesty of purpose and of speech. But through it all there shone the deep devotion of a man to his duty."

We, his colleagues in obstetrics and gynaecology, mourn the loss of a great figure in our speciality. For what James Hendry accomplished, for his friendship, for his cameraderie, we place on record our heartfelt thanks. And in doing so we trust that this expression of our admiration may in some small measure bring comfort to Mrs. Hendry, as we feel sure it will be a source of pride and inspiration to their three sons.

JOHN MUNRO KERR.

Any account of James Hendry which did not lay stress on his virtues as a friend, his charm as a companion and his ability as an examiner would be incomplete.

I was privileged to be amongst his friends for over 20 years, a friendship which speedily grew into affection.

He was kind, generous and staunch. One could discuss anything with him with confidence and his advice on matters of practice, hospital problems, or University or personal affairs was always of value. He had a marvellous faculty of seeing the essentials of any subject and in discussion could put his points with a clarity which was the mark of a first class and at the same time practical brain.

It was a delight to travel with him on the Continent, which was my happy experience on numerous occasions as a fellow member of the Gynaecological Visiting Society. His organisation of our last two foreign journeys before the war—to Vienna and Budapest and Hamburg and Berlin—won for him the gratitude of the Society, while his fluent German gained our admiration and smoothed our way.

We were associated for 8 years as co-examiners in Glasgow and Belfast. In the past 25 years I have had many able and delightful colleagues but none to excel him. He was direct and practical; his questions clearly framed, varied and well expressed. Always courteous, the end of even the longest day found him alert, patient and good tempered. He had an unfailing instinct for the candidate with his goods in the window and speedily probed the depth of his knowledge.

Many happy memories are evoked by our evenings in both cities. Dining, either alone or with colleagues, he was a most agreeable and congenial host or companion. Blessed with a prodigious memory and a mine of general information, especially about his native Ayrshire and its links with Ulster, those evenings are the source of many a happy memory. In Belfast, as in

Glasgow, his colleagues sincerely mourn his death.

The sympathy of all who knew him, and especially those who enjoyed the hospitality of his happy home will go out to Mrs. Hendry and to his three soldier sons, the second of whom is a member of our profession.

C. G. LOWRY.

It is hard to realise that James Hendry has really gone from among us and that he will no longer guide the destinies of obstetrics in Glasgow. To those closely associated with him he always gave the impression of tireless energy and enduring strength, which enabled him to accomplish successfully an amazing amount of work—a busy consulting practice, the exacting duties of teaching and administration associated with a University Chair, and invaluable service on hospital and national committees of one sort or another. In addition, he was always accessible to every student and young graduate, who sought advice or help. As his senior assistant for 9 years I know what a deep, personal interest he took in junior obstetricians, whether on his own staff or not. He encouraged us to attend and take part in the various medical societies' meetings, at which he was a constant attender; and we will remember those winter nights when he took us to the meetings of the Edinburgh Obstetrical Society, motoring home to Glasgow after midnight, when he was very much fresher than his juniors.

He was a very shrewd judge of character and this enabled him to choose his staff wisely. He greatly valued willing, loyal service and was most considerate of the feelings of all who worked under him down to the most junior nurse. As a result, he had the devotion of his ward sisters and nurses, whose main thought was the efficiency of the unit under an inspiring Chief.

His sound judgment, combined with an extraordinarily wide range of experience, made him an outstanding clinician and this was reflected in his brilliant teaching.

He was constantly thinking of the future, but unlike many planners, his plans were always workable and he knew how far it was practical to go. He had a driving force given to few men. He will be universally missed and by none more than his University in these days when someone with his qualities and experience is so sorely needed. I should like to record on behalf of all his assistants our particular sense of loss, since apart from gratitude for all he taught us, he was our constant counsellor and friend.

DUGALD BAIRD.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of the Council was held in the College House, on Saturday, 28th July, 1945, with the President, Mr. Eardley Holland, in the Chair.

Mr. Eardley Holland was re-elected President to take office in October next.

The following officers were also elected:

Vice-Presidents:
Professor D. Dougal.
Professor R. Marshall Allan.

Honorary Treasurer: Mr. W. Gilliatt.

Honorary Secretary: Mr. G. F. Gibberd.

Honorary Librarian: Mr. F. W. Roques.

Honorary Curator of Museum: Mr. A. W. Bourne.

The following candidates were elected to the Membership:

Trevor Montagu Barnett.
Alexander Buchan.
Daphne Wai Chan Chun.
Aileen Marian Dickins.
Ernest Dudley Yarnold Grasby.
Michael Willoughby Hemans.
Ursula Mary Lister.
Agnes Macfarlane Duncan Milne.
Abd-El-Salem Mahmood El-Minabbawy.
Kripananda Mitra.
Joan Pudsey Moignard.
Padma Raj.
Wallace Beresford Shute.
Beatrice Marian Smyth.
James Macbeth Thomson.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

Any inquiries should be addressed to Miss D. F. Atkins, British Postgraduate Medical School, Ducane Road, London, W.12.

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